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Table of Contents.

Listerian Oration.[1]

THE SEED AND THE SOIL: HOST SUSCEPTIBILITY IN INFECTIOUS DISEASES.

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ONE hundred years ago Joseph Lister was undergoing his surgical apprenticeship with Syme in Edinburgh. Being a thoughtful young man he could not but be impressed by the awful consequences which frequently followed the surgical procedures in which he was acquiring such technical skill, for breach of the skin led more often than not to surgical infection. Although the orthodox view at that time was that surgical infection, like other infectious diseases, was the result of vague environmental influences, or of the patient's constitutional diathesis or the state of his humours, the climate of opinion in western Europe was being prepared for the germ theory of disease. In 1836 Bassi had shown that fungi caused a fatal disease in silkworms, and a few years later Schönlein had recognized the fungal ætiology of ringworm. Between 1855 and 1860 Pasteur was engaged on his masterly demonstration of the microorganismal basis of fermentation. Although he had not yet extended his experimentation to animals and man, Pasteur had clearly envisaged the role of microbes in infectious diseases, as had Bassi a decade earlier. Thus the practical demonstration by Lister that the use of antiseptics in surgery would prevent surgical infection came to a receptive public, whereas Semmelweiss's application of the same principles in maternity hospitals in Hungary almost twenty years earlier was first ridiculed and then ignored.

The final triumphant demonstration of the truth of the germ theory of disease came with the work of Pasteur and Koch between 1867 and 1881; and application of these principles to protozoal, bacterial, rickettsial and viral diseases resulted in the discovery of the specific agents responsible for the vast majority of infectious diseases. The Pasteurian revolution is now virtually complete—a revolution ignored by earlier historians, but quite as important in its consequences as the industrial revolution, for it has made food and not disease the ultimate limitation of human breeding.

[1] Delivered at a meeting of the South Australian Branch of the British Medical Association on April 24, 1958.

The virtual elimination of the great epidemics and the effective control of most of the killing infectious diseases can be described as the conquest of infectious disease; and when one considers man as an animal, and the factors which control his evolution, that is a reasonable interpretation. But as all of you who practise medicine know, infections of diverse kinds still cause a great deal of intermittent morbidity and chronic ill-health. Although as students of human evolution we may say that the infectious diseases are no longer of importance, as doctors we cannot regard with complacency the ill-health and the suffering occasioned by non-fatal infections.

The early microbiologists, obsessed with the necessity for demonstrating the specificity of infectious diseases, paid scant attention to the old doctrines of the constitutional diathesis and the state of the bodily humours. Today we can look more dispassionately at the problem; the importance of the seed is universally accepted, so that we can consider more closely the soil on which the seed falls.

All multicellular living organisms are complex assemblages of a variety of cells specialized for different functions; they are also complex associations of a number of different organisms. Consider the multitude of parasites and symbionts in a tree—the roots invaded by fungi and bacteria, the leaves parasitized by bacteria, fungi and viruses, and the trunk host to a wonderful variety of insects. Or a man, with bacteria and protozoa inhabiting his gut and bacteria on his skin, to say nothing of the bacteria, protozoa and viruses now being demonstrated in his internal organs. If we look more closely we realize that some of these microorganisms were recognized as the specific agents of infectious diseases years ago, yet the hypothetical man we are studying is in what we regard as normal health. With the ubiquitous parasites associated with endemic infections we are driven to recognize the difference between infection and disease, the one condition very common, the other relatively rare.

In order to investigate experimentally the interaction between two different living things, each of which may vary independently, we must deal with two abstractions—the constant host and the varying microbe, and the constant microbe and the varying host—rather than try to assess the full complexity of the natural interaction. Indeed, for both host and parasite we must consider both genetic and environmental aspects. In detail, the interaction between parasite and host may be conditioned by (i) the genetic nature of the infective agent (that is its intrinsic virulence), (ii) the physiological state of the infective agent at the initiation of infection, (iii) the genetic constitution of the host animal (that is its intrinsic susceptibility), (iv) the physiological condition of the host animal (including as a special aspect past experience of the host with immunologically similar infective agents).

Genetic Constitution and Physiological State of the Parasite.

Two examples derived from the study of tuberculosis will suffice to illustrate the importance of the genetic constitution and physiological state of the infective agent. The laboratory strain of human tubercle bacilli known as H37Ra is an avirulent derivative of H37Rv, a highly virulent strain. H37Rv kills experimental animals; H37Ra fails to multiply in them. This difference in intrinsic virulence depends upon genetic differences between H37Rv and H37Ra.

However, the virulence of H37Rv is also affected by its physiological state. This is best illustrated by Bloch's work on the relative virulence of similar doses of H37Rv taken during the lag phase, during logarithmic growth, and during the stationary phase of growth in a liquid medium. For a constant dose, counted on a bacteriological plate, the bacteria were of minimum virulence during the lag phase and maximum virulence during the logarithmic phase. Further, if bacilli at any stage of growth were treated with petrol-ether they remained viable (when tested on bacteriological media), but failed to initiate infection in experimental animals unless large doses were used. Thus both the genetic nature of the infective agent and its physiological state affect its virulence.

Genetic Constitution of the Host.

There are, of course, profound genetic differences between different species of animals, and these condition species-susceptibility to infective agents. Tonight, however, I am concerned with differences between individuals or between races or strains of the same species of host animal.

Strain Differences in Response to Infection.

Its convenience has made the mouse, from the genetic standpoint, the most extensively investigated of all mammals. Many different pure lines of mice, derived by long-continued brother-sister mating, are available; and selective breeding has been carried out to obtain strains highly susceptible or highly resistant to different bacteria and viruses.

The pioneer work in this field was carried out by Webster between 1930 and 1940. He showed conclusively that the most important factor governing the fate of mice exposed to mouse typhoid infection in experimental epidemics was the genetic constitution of the host animals. When the infective agent was introduced into populations of previously non-exposed, but genetically resistant and genetically susceptible mice, fatal cases occurred almost exclusively in the genetically susceptible animals. Concurrent tests of these mice showed that susceptibility to St. Louis encephalitis virus was inherited quite independently of susceptibility to mouse typhoid.

In addition to this clear definition of the role of genetic factors in the response to infection, Webster made some preliminary studies of the mechanisms underlying innate resistance to virus infections. The level of viral multiplication after intracerebral inoculation of St. Louis encephalitis virus in genetically resistant mice was only one-thousandth as high as after similar inoculation into susceptible animals. That this difference was due to a difference in the cells in which the virus multiplied was demonstrated by tissue-culture experiments. Brain tissue obtained from genetically susceptible mice promoted virus multiplication to much higher titres than that obtained from resistant animals.

Understanding of the mechanisms of the innate resistance of certain strains of mice to virus inoculated into the brain was further advanced by the observation of Albert Sabin that mice of the Princeton Rockefeller Institute colony (PRI mice) showed an unexpectedly low susceptibility to 17D yellow fever virus. Sabin has not yet presented a complete genetic analysis of the situation, but the following important facts have emerged: (i) Resistance to 17D yellow fever virus depends on dominant autosomal genes which depress the level of viral multiplication to 0·01% of that occurring in susceptible mice. Although preliminary breeding experiments suggested a single pair of autosomal genes, the operation of multiple genes with a small amount of crossing over was not excluded. (ii) the genetic multiplication-depressing factor exerted its effect on several immunologically related viruses (yellow fever, dengue, West Nile, Japanese B, St. Louis and Russian encephalitis), but not on other unrelated encephalitis viruses. (iii) Experiments with tumours implanted in susceptible and resistant mice showed that the multiplication-depressing factor was localized to cells of the susceptible animal and was not transferred to the tumour cells. (iv) A second factor also affected the resistance of mice; this was the level of cellular vulnerability to the effects of the virus. For some viruses high cellular vulnerability was observed in very young mice, whereas in adults of the same strain cellular vulnerability was low. Other strains of mice showed high cellular vulnerability at all ages.

Many other examples are now available of the differences in the response of different strains of mice to infection with protozoa, bacteria and viruses. Nadel, for example, found clear-cut differences in the survival time of different strains of mice after the intravenous inoculation of *Plasmodium berghi*, and several investigators have reported similar results with *Mycobacterium tuberculosis*. Where it has been investigated by the study of F1 hybrids and backcrosses, the differences between strains appear to be due to complex genetic factors.

Host Genetic Factors in Infectious Diseases of Man.

The interest and importance of these experimental studies in animals, for those of us interested in human medicine, is the light that they may shed on the interaction of the human host with its parasites. Obviously they give considerable support for the view that the genetic constitution of the host animal is a major factor in the host-parasite relationship.

What direct evidence is there from human medicine? Two types of information are available. First there are the comparisons of the reactions of different human races to various infectious agents. Of course, human races are by no means as genetically homogeneous as are inbred strains of mice, so that one must expect a rather wider spectrum of response than was found with inbred mice. Considerable difficulties arise in the interpretation of data purporting to show that different races vary in disease susceptibility, due to a large extent to complications introduced by active immunization and by different social conditions. Nevertheless, few will dispute the different susceptibilities to leprosy and tuberculosis, for example, of population groups with long histories of exposure to these diseases, and of other groups which meet them for the first time.

A second and more powerful technique which allows a more direct assessment of the role of genetic factors in man is the twin-study method, originally conceived by Francis Galton. The technique here is to study the responses of twin pairs to various infective agents. If proper allowances can be made for active immunization of one member of the pair the comparison of non-identical with identical twins provides direct evidence of the importance of genetic factors. So far the best information of this type relates to tuberculosis. Somewhat less convincing evidence has been presented on inherited resistance to paralytic poliomyelitis.

Though not the first, the study by Kallman and Reisner on tuberculosis in twins in New York State provides the most extensive and convincing data. Of course, tuberculosis cannot occur in the absence of infection, but the twin studies emphasize the importance of genetic factors in the conversion of infection into disease. When morbidity rates were adjusted to allow for the different ages of the individuals examined, Kallman and Reisner found that the likelihood of the subjects developing manifest tuberculosis increased in strict proportion to the degree of blood relationship to a tuberculosis index case, the relevant corrected rates being 7·1% for marriage partners, 25·5% for full siblings, 25·6% for dizygotic co-twins, 87·3% for monozygotic co-twins. These results leave no doubt as to the importance of "constitution" in tuberculosis; doubtless the method would have been applied on a wider scale than it has to other diseases if suitable index cases were more common.

Attention should also be drawn to two situations in which large differences in the susceptibility of human populations to certain virus diseases may be due to differences in genetic resistance. They are certain virgin-soil epidemics of poliomyelitis, and of yellow fever in native Africans and South Americans. Virgin-soil epidemics of poliomyelitis in isolated communities often show very high paralysis rates and high death rates. A multitude of factors may influence such situations—the different responses of young and adult individuals, the possible effects of cross immunity due to previous infections with other strains, and the stresses thrust on isolated communities by epidemics of disease. It is well to consider also the possibility, first pointed out by Sabin, that continued inbreeding in the absence of virus might have resulted in the development of populations of special genetic susceptibility.

Yellow fever is enzootic in the forests of Africa and South America. In Africa native man and monkey appear to be highly resistant to infection, although cases in Europeans show that the virus is of high virulence. In South America there is a much wider spectrum of resistance in both man and monkeys, severe infections being not uncommon. A plausible explanation is that Africa is the ancestral home of the disease, and over many generations natural selection has virtually eliminated susceptibles from the population. The virus was probably carried to South America by ships engaged in the slave trade, and not enough time has elapsed for natural selection to have greatly reduced the genes for susceptibility.

There is only one case in which it has been possible to study the time scale of natural selection for genetic resistance, and that is myxomatosis in the Australian wild rabbit. Here the situation in 1950 was that the virus was of very high virulence and the rabbits of uniformly high susceptibility, so that in natural epizootics all cases were severe, and only about two animals recovered out of every thousand infected. For reasons I have described elsewhere, viruses of lower virulence (causing about 90% mortality rates in laboratory rabbits) soon became dominant, but there have also been progressive changes in the genetic resistance of the wild rabbit population. These have been most pronounced in areas subjected to annual severe epidemics. The changes have been demonstrated by catching susceptible young rabbits each spring for several successive years, raising them to adulthood in protected laboratories, and challenging them with a slightly attenuated virus which has been stored in dry ice since 1953. The average mortality rate fell from an initial level of 90% to 50% within four years, that is four successive episodes of disease, and breeding from the survivors. We would not expect natural selection to eliminate susceptibles as rapidly as this in most infectious diseases, because the mortality rates are much lower. But it is apparent that the elimination of highly susceptible individuals before the reproductive age might well explain the differences I described earlier between the reactions of different human populations to a number of infectious diseases.

Genetic Abnormalities in Man which Affect the Response to Infective Agents.

Recently, several genetic abnormalities have been described in man which have a profound effect on the response to infection. Such are agammaglobulinæmia, abnormal hæmoglobins and acatalasæmia.

Agammaglobulinæmia.—Agammaglobulinæmia was first recognized in 1952. I will consider only the congenital form, which appears to be inherited in much the same way as classical hæmophilia, that is as a recessive character appearing in male children and transmitted through phenotypically normal females. Case histories indicate recurrent bacterial infections, and investigations show almost complete absence of γ globulin and isohæmagglutinins, as well as an absence of plasma cells in the bone marrow and lymph nodes. There are some puzzling features in the responses of these children to infection—features which when elucidated will certainly enlarge our understanding of both antibody production and the mechanism of recovery in bacterial and viral diseases. The dominant clinical feature of these cases has been the frequency of bacterial infections, and indeed none of the children could have survived before the antibiotic era. The response to virus infections presents different patterns in different cases. In some, diseases such as chickenpox and measles follow much the same course as in normal children—which makes it difficult to sustain the conventional view that recovery is a function, at least to some extent, of antibody production. Smallpox vaccination either follows the same pattern as in normal children, that is it is self-limited and is followed by an "immune" (allergic) response three months later, or else vaccination leads to generalized vaccinia. In the latter cases it is significant that all the secondary lesions follow the same course of development as the primary—there is no evidence of an accelerated or allergic response. In cases tested, tuberculin sensitivity appears to develop in the usual way after BCG vaccination, and in one or two cases homologous skin grafts (which never take in normal subjects, unless they are identical twins) have remained intact for as long as three years. These varied results suggest that, as in the case of the abnormal hæmoglobins of which I will speak in a moment, agammaglobulinæmia comprises several different genetic defects as yet undifferentiated. Certain it is that intensive study of such cases may provide more information about the role of the antibody mechanism in infectious diseases than a decade of experimental work with animals; and by its nature agammaglobulinæmia is a defect which can be recognized only in man.

Abnormal Hæmoglobins.—It has long been known that sickle-cell anæmia is a genetic disease, occurring with varying frequency in Negroes from different parts of Africa. Individuals homozygous for the sickle-cell gene suffer from a hæmolytic anæmia; heterozygotes suffer no such disease, but can be recognized by examination of their blood. Pauling and Itano in 1949 opened a new chapter in the study of genetic diseases of man by their demonstration that the hæmoglobin associated with sickle-cell anæmia (hæmoglobin S) differed chemically from normal hæmoglobin; and since then a variety of genetically determined abnormal hæmoglobins have been recognized in man.

While most of these are quite rare, the sickle-cell gene is very common in some parts of Africa, where up to 40% of the population may be heterozygotes, although the homozygous condition causes high mortality in childhood (from anæmia), and the genetic fertility of sickle-cell homozygotes is only one-quarter that of the heterozygotes. This poses an interesting problem, for it has been calculated that to replace the loss of sickle-cell genes by mutation alone would necessitate a mutation rate of 10^{-1} per gene per generation, that is a rate about 5000 times greater than other estimated mutation rates in man. Further, the restriction to one or two human races, and the patchy distribution of the gene within these races (rates in neighbouring tribes in Africa vary from nil to 45%) are inexplicable by mutation alone. There appears to be a state of what is called balanced polymorphism, in which the heterozygote is better adapted for survival than either homozygote, that is than either those homozygous for hæmoglobin S (who often die from hæmolytic anæmia) or those homozygous for normal adult hæmoglobin. Allison and Raper have recently suggested that the selective agent is falciparum malaria—an attractive idea because of the fact that malaria parasites subsist on hæmoglobin. They support their claim by comparisons of the high incidence of heterozygotes in the malarious parts of Uganda and the low incidence in non-malarious areas, by the equal rate of occurrence of uncomplicated malaria in normal children and sicklers, by the great preponderance of cases of cerebral malaria and blackwater fever in the normal children, and by some experiments on parasitæmia after the inoculation of *P. falciparum* in children with and without the sickle-cell trait. The situation is not a simple one, because another abnormal hæmoglobin (C) is also known to be patchily distributed in Africa and affects the rate of elimination of sickle-cell genes from the population. Nevertheless, bearing in mind the high mortality rates of falciparum malaria in untreated children, Allison's suggestion appears to be sound, and to provide us with a beautiful example of a mechanism by which genetic constitution can affect the severity of an infectious disease, and a mechanism by which genes which appear at face value to be highly undesirable may be perpetuated.

Haldane has pointed out that this example is a double paradox: on the one hand an infectious disease (malaria) has been responsible for the spread of a congenital disease not obviously related to it. On the other hand, chemotherapy, instead of allowing more genetically defective individuals to survive, will in time lead to a disappearance of the congenital disease.

Acatalasæmia.—An intriguing genetic abnormality which affects resistance to recurrent oral ulceration was described a few years ago by Takahara in Japan. When he was treating such a case with a hydrogen peroxide mouthwash he found that the fluid turned brownish black instead of bubbling. It has been known for years that, if hydrogen peroxide is added to normal blood, oxygen is evolved and the colour of the blood remains normal, because the catalase present decomposes the hydrogen peroxide to water. On testing blood from his patient and two siblings who also had oral ulcers, Takahara found that catalase was absent from their blood. The familial distribution of the abnormality suggested its genetic basis. The increased susceptibility to oral infection is probably due to local anaerobiosis produced by hæmolytic streptococci, which are the predominating organisms in these lesions.

Physiological State of the Host.

I cannot hope to cover adequately all aspects of this enormous subject tonight. Quite apart from classical acquired immunity, which is after all a physiological response of the host animal, there are a vast number of differences in host physiology which affect the response to infectious agents.

The Influence of Age on the Manifestations of Disease.

The most obvious implications of age are concerned with passive and active immunization, but in this section I am concerned with the way in which the intensity of illness varies with age in non-immune individuals. This was discussed at some length by Burnet in his Charles Clubbe Memorial Oration in 1952, and the remarks which follow are largely derived from this paper. If we exclude infection *in utero*, the general picture in man may be summarized as follows.

1. The younger the child the more likely is exposure to an infective agent to be followed by infection, and the more likely is an intrinsically virulent microbe to produce death. All of us are aware of the serious nature of tuberculosis, pertussis, diphtheria and the common infectious diseases in infants. Poliomyelitis, on the other hand, seems to be notably less severe in very young infants. Not only are paralytic cases rare in tropical communities where infection is universal by the end of the first year of life, but also in a few well studied virgin-soil epidemics in the Pacific Islands and in Eskimos "everyone except the babies had symptoms".

2. Where symptoms and death are due mainly to the inflammatory response rather than to actual damage to infected cells, these tend to reach a maximum in the young adult. The classical example was influenza in the 1918-1919 pandemic, but the young adult peak in susceptibility to tuberculosis and, in military recruits, to mumps and measles are other examples in which the non-immune young adult appears to be more susceptible than the child, though usually less so than the infant.

3. In the absence of immunity, the mortality of infections contracted in later life progressively increases with age.

Hormonal Effects on the Response to Infectious Agents.

Some of these age effects may well have a hormonal basis, and the great increase in susceptibility to many infectious agents which occurs during pregnancy is also associated with the hormonal changes occurring then. The recent introduction of cortisone into clinical and experimental medicine has provided abundant examples of the influence of this hormone on both bacterial and viral infections. In general, overdoses of cortisone enhance susceptibility to bacterial and viral infections, and often allow latent bacterial or viral infections to produce manifest disease. Cortisone affects both the inflammatory response of the host and the antibody response and also causes alterations in the metabolism of tissue cells. Its enhancing action may therefore be due to a combination of several different types of metabolic disturbance.

Associations of Different Infections.

One common and important way in which the host may be rendered more susceptible to certain infectious agents is the occurrence of other infections. You are all familiar with the potentiation of bacterial respiratory disease by infections with influenza and measles viruses, and those of you who treated soldiers in World War II will remember how an attack of bacillary dysentery often paved the way for the pathogenic action of *Entamœba histolytica*. In both cases the explanation is probably that the first infection so alters the surface cells of the respiratory or intestinal tract that the normal defence mechanisms against secondary bacterial or protozoal infection fail to function effectively.

The Effect of Local Vascular Changes on the Establishment of Infection.

The existence of acquired immunity complicates most attempts to analyse the nature of natural resistance to infections. One method of overcoming this experimentally

is to focus attention on the events which occur within the first few hours after the lodgement of the infective agent in the body. Some of the most informative experiments are those conducted by A. A. Miles on the effects on the establishment of bacterial infections of substances which modify vascular physiology. Perhaps the most clear-cut example is the effect of adrenaline on intradermal infections of guinea-pigs. When bacteria are injected intradermally in guinea-pigs they produce their maximum effect 24 to 48 hours later in local lesions, the size of which depends upon the dose. Miles found that doses of adrenaline which had no effect on the bacteria *in vitro*, or on the bactericidal effect of blood, might have profound effects upon the infectivity of bacteria inoculated into the skin. Depending upon the species and the strain of bacteria, such a dose of adrenaline given with the inocula enhanced infectivity from tenfold to ten-millionfold. By making the adrenaline injection at the same site, but at various intervals after the injection of bacteria, it was found that the decisive period was four or five hours. In the doses used, adrenaline causes local vasoconstriction for two or three hours, thus diminishing the local supply of hormonal and cellular constituents of the blood. Miles's experiments demonstrate the importance of these local factors (phagocytosis, bactericidal activity of blood, etc.) in destroying large numbers of the inoculated bacteria within the first few hours after their introduction. As might be expected, the effect was found to extend to the ultimate lethal effect several days later; simultaneous injection of adrenaline was found to enhance the ultimate lethal effect of group C streptococci in mice a hundredfold, but injected into local streptococcal lesions four hours after the streptococci it had no effect.

Latent Infections.

I pointed out earlier that when the germ theory of infectious disease was formulated in the nineteenth century, lethal infections and disastrous epidemic diseases dominated men's minds. With the virtual elimination of these in the western world, it is necessary for us to look again at the problems posed by infectious diseases. We see that in the latter half of the twentieth century the emphasis has shifted from lethal epidemic diseases to the endemic infections, which are characterized by ubiquity of infection, but by the relative rarity of overt disease. This brings us to the problem of latent infections and of the conditions which may alter the host-parasite balance so that infection becomes disease. Here we encounter situations in which physiological changes in the host animal rather than genetic differences between host animals are of over-riding importance, although, of course, physiological change must always be affected by the genetic background against which it operates.

Measles is perhaps the best defined of all infectious diseases. It is always possible to trace a case to a known contact; infection virtually always produces distinctive symptoms and recurrences are unknown. At the other extreme are such conditions as cytomegalic inclusion disease and toxoplasmosis, in which recognized cases of disease are extremely rare and are confined to the newborn, yet serologic surveys show that infection is very widespread in adult human populations.

The vast majority of human infections fall between these two extremes. Infection with tubercle bacilli is almost universal, but tuberculosis is uncommon. Pathogenic staphylococci are ubiquitous, but only occasionally do they give rise to mild or severe disease. I need not multiply instances in which infection cannot be equated with disease, but I should perhaps differentiate two types of non-symptomatic infections—the inapparent acute infection and the chronic latent infection. In the one case the infectious episode, as judged by laboratory tests, is analogous to an attack of measles, but there are no recognizable symptoms. Like measles, however, recurrence at either a symptomatic or non-symptomatic level is unknown. Chronic latent infection may be preceded by obvious disease, as in primary herpetic stomatitis, or there may be no disease at the time of lodgement of the infective agent, which may remain latent in the body for many years or may be activated by some alteration in host physiology.

The precise mechanisms by which latent infections can be converted to active disease are unknown, but two obvious possibilities can be readily disposed of. First, activation of the infectious process does not appear to be the result of the loss of specific protective immunity. The development of cold sores by the herpetic individual is unrelated to the level of neutralizing antibodies to herpes virus. Second, there is no change in the intrinsic virulence of the latent agent, either in viral diseases like herpes and psittacosis or bacterial diseases like tuberculosis. The most convincing demonstration of the latter point comes from Vorwald's experiments on tuberculosis due to BCG in silicotic guinea-pigs. After vaccination, living BCG bacilli persist in the animal body for long periods. If vaccinated guinea-pigs inhale silica dust they develop tuberculosis, yet the bacilli recovered from their lesions are just as attenuated as those originally injected.

Latent microorganisms may be "provoked" to activity in many different ways. The stresses and hormonal activity associated with reproduction and lactation may activate agents as diverse as tubercle bacilli, the Bittner virus of mammary carcinoma of mice, and toxoplasma. Large doses of cortisone and intense radiation can enhance many types of infectious process, in a variety of animals. Herpes simplex virus may be provoked by attacks of fever, by menstruation or by exposure to sunlight. Extreme malnutrition may be associated with enhancement of the activity of a wide variety of infectious agents. Injections of endotoxin derived from Gram-negative bacteria may in turn enhance and depress the resistance of mice to a wide variety of bacterial pathogens. The scanty evidence available suggests that endotoxin acts through its effects on the cells of the reticulo-endothelial system.

Most of the effects I have just described operate independently of specific acquired immunity. I mention this not to minimize the importance of acquired immunity in resistance to infection, but to emphasize the fact that, in the latent infections I am chiefly concerned with at the moment, non-specific non-immunological factors are probably of greater importance than specific antibodies.

The most comprehensive attack on these problems comes from the laboratories of R. J. Dubos in New York, and what I shall have to say in the following sections is largely derived from his work.

All the methods of "provocation" mentioned earlier lead to changes in host physiology. From the point of view of activation of latent infectious agents it is important to realize that they are localized in the neighbourhood of small groups of cells in special parts of the body. Their relations with these cells may vary: they may be obligate intracellular parasites; they may survive in areas of necrotic tissue; certain of the viruses may be as intimately associated with the host genome as prophage is with the bacterial chromosome. Diverse methods of provoking latent infections may thus operate through a relatively small number of changes at the cellular level. Unfortunately, our knowledge of intracellular physiology, the physiology of the micro-environment of the latent infectious agent, is still rudimentary. However, it may be useful to describe one or two of the "final common pathways" whereby various physiological insults can affect the micro-environment of the parasite.

Phagocytosis is demonstrably an important host reaction in bacterial infections. Leucocytes can produce large amounts of lactic acid, and their intracellular pH after phagocytosis is probably low, as is the pH of inflammatory exudates. These conditions, both *in vitro* and *in vivo*, are bacteriostatic or bactericidal for some bacterial pathogens, but have little effect on others. In addition, the varied vascular changes of inflammation greatly reduce the local oxygen supply and increase the carbon dioxide tension. And if necrosis occurs a great variety of substances are released, many of which profoundly affect the fate and behaviour of pathogenic agents.

The physico-chemical characteristics of the micro-environment of infectious agents depend ultimately on the biochemical activities of tissue cells, which in turn vary with the metabolic state of the individual. Thus one may mention the ketosis of uncontrolled diabetes or starvation, the low glycolytic activity of leucocytes in diabetics, and the altered metabolism of tissue cells to which cortisone has been added *in vitro*. Uncontrolled diabetes and acute star-

vation are associated with greatly increased susceptibility to infection, which disappears when the patient is returned to health; that is the susceptibility to infection appears to be due to a reversible biochemical disturbance in the tissue cells which constitute the micro-environment of the infective agents, or perhaps in the extracellular fluids.

The environmental factor most frequently suspected of altering resistance to latent infections has been malnutrition, yet attempts to demonstrate experimentally a relationship between malnutrition and the activation of infectious disease have been, on the whole, unsuccessful, probably because the problems were incorrectly formulated. Experiments by Dubos have shown that chronic malnutrition as such has no effect on resistance to bacterial infections, and there is a good deal of experimental evidence to show that undernourished animals are more resistant than normal animals to viral infections. On the other hand, if mice are starved for two days before infection with staphylococci or tubercle bacilli, and given glucose-saline to drink, they are much more susceptible than control animals. This effect is rapidly reversible, for two days' free feeding on a normal diet restores the normal level of resistance.

One of the best examples of the relation between nutrition and susceptibility in human infectious diseases comes from the study by a group of Danish physicians of starvation amongst Danish prisoners of war in German concentration camps during World War II. Among young men who belonged to the police force and the resistance movement, and who came from a country with high nutritional standards and low tuberculosis rates, severe tuberculosis was relatively common after exposure to semi-starvation, but when these men were returned to a favourable environment they usually recovered, without the help of chemotherapy. There is a suggestion from this work, as from the experimental studies, that only when malnutrition reaches an extreme degree does it increase susceptibility to tuberculosis. The real link between nutrition and infectious disease may be metabolic disturbance rather than specific nutritional deficiencies.

Though little is known about the activation of latent bacterial infections, even less is known about the latent viral infections. The example of lysogeny in the bacterial viruses, in which it has been clearly demonstrated that prophage, the ultimate genetic determinant for phage production, is located on specific portions of the bacterial chromosome, has induced considerable speculation about comparable situations with animal viruses. So far "virogeny" has been suspected with the Shope papilloma virus, with herpes simplex virus, and recently with some of the adenoviruses, but conclusive proof in these cases is still lacking. An important implication of the concept of virogeny is, of course, the virus origin of some forms of malignancy, so that with viruses problems of latency have even greater importance than in bacterial infections. It is significant that the only demonstrated case of virogeny among the animal viruses is the virus-induced malignant tumour of chickens, Rous sarcoma.

Surgery has moved far since the days of Lister. Asepsis, antibiotics, blood and electrolyte therapy and anæsthesia have removed the barriers which formerly baulked the surgeon's skill. In the "medical" infectious diseases also, the picture has altered drastically since Lister's day. We are not now concerned with the great plagues or the lethal epidemics; these are under control. But there is a vast residue of minor illness due to microbial pathogens and perhaps also to microorganisms not usually regarded as pathogenic. Degenerative and neoplastic diseases, in which the role of microbes awaits proper evaluation, have assumed a much greater importance due to the prolongation of the life span of man. Students of infectious disease must therefore move from the nineteenth century preoccupation with the great killing diseases and the relatively simple picture of infection leading immediately to disease (of severity varying from lethal to subclinical). They must look more thoroughly at the endemic infections of the present, studying the microbes from biochemical and genetic points of view, and the host also from the viewpoints of the geneticist and the experimental pathologist. Only in this way may man eventually be able to come to terms with his microbes, not by using a *therapia magna sterilisans*, but by understanding the genetic bases of host susceptibility and by designing procedures for metabolic control, which may enable man to live at peace with those of his microbes which are an inescapable part of his environment.

Specific preventive vaccination alone will not be the answer to many of the endemic infections I have discussed tonight, nor will chemotherapy. The much more difficult process (on a global scale) of the steady improvement of social conditions seems to be the essential prerequisite to the eventual conquest of the infectious diseases.

THE USE OF ACTH IN THE DIAGNOSIS OF ADDISON'S DISEASE.

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Although Addison's disease, with its striking classical symptoms, is the best-known example of adrenal cortical insufficiency, great difficulty may be experienced in establishing the diagnosis in some patients. None of the individual signs of the disease may be considered as pathognomonic of adrenal cortical insufficiency, since pigmentation, hyponatræmia and hyperkalæmia all occur in a wide variety of conditions unassociated with Addison's disease. Furthermore, difficulties in diagnosis may be increased since, under normal conditions, there is no single laboratory estimation that can unequivocally establish the presence of the disease.

The number of laboratory tests for adrenal failure is considerable (Bland, 1956), but there can be no doubt that the most successful procedures are those based on the effect of ACTH on the excretion of urinary steroids (Thorn, Goldfien, and Nelson, 1956; Prunty, 1956; Nabarro, Moxham, and Walker, 1957). Unchanged levels of urinary 17-ketosteroids (17-KS) and 17-hydroxycorticosteroids (17-OHCS) following ACTH treatment provide the surest evidence of Addison's disease.

The development of routine procedures for the determination of urinary 17-OHCS (Norymberski, Stubbs, and West, 1953; Porter and Silber, 1950) has lent invaluable aid to the clinical investigation of adrenal cortical function (Laidlaw, Reddy, Jenkins, Haydar, Renold, and Thorn, 1955; Hubble, 1955; Levell, Mitchell, Paine, and Jordan, 1957; Moxham and Nabarro, 1956). Several clinical ACTH tests have been described, differing mainly in the method of corticosteroid determination and mode of ACTH administration (Jenkins, Forsham, Laidlaw, Reddy, and Thorn, 1955; Engbring, Truitt, and Engstrom, 1956; Prunty, 1956; DeFilippis and Young, 1957).

In this paper the use of an intravenous ACTH test is reported, in which adrenal cortical function is assessed primarily from urinary 17-OHCS excretion, and secondarily from the excretion of sodium and potassium. Results of applying the test to patients with symptoms of Addison's disease are presented, and a comparison is made with the water excretion test of Kepler, Robinson and Power (1942). The efficacy of the ACTH stimulation test is illustrated by the detection of a case of Addison's disease caused by adrenal amyloidosis, a condition that is rare and difficult to diagnose (Cope and Woodrow, 1953).

Materials and Methods.

In the few cases in which the effect of a single day's treatment with ACTH was studied, the hormone was given intravenously over six hours. Urine was collected for steroid and electrolyte analyses at three-hourly intervals before, during and after administration of ACTH.

In the longer studies, urine was collected for one or two 24-hour periods to establish control values for the excretion of steroids and electrolytes. ACTH was given on two or more days, each infusion lasting eight hours. Daily urine

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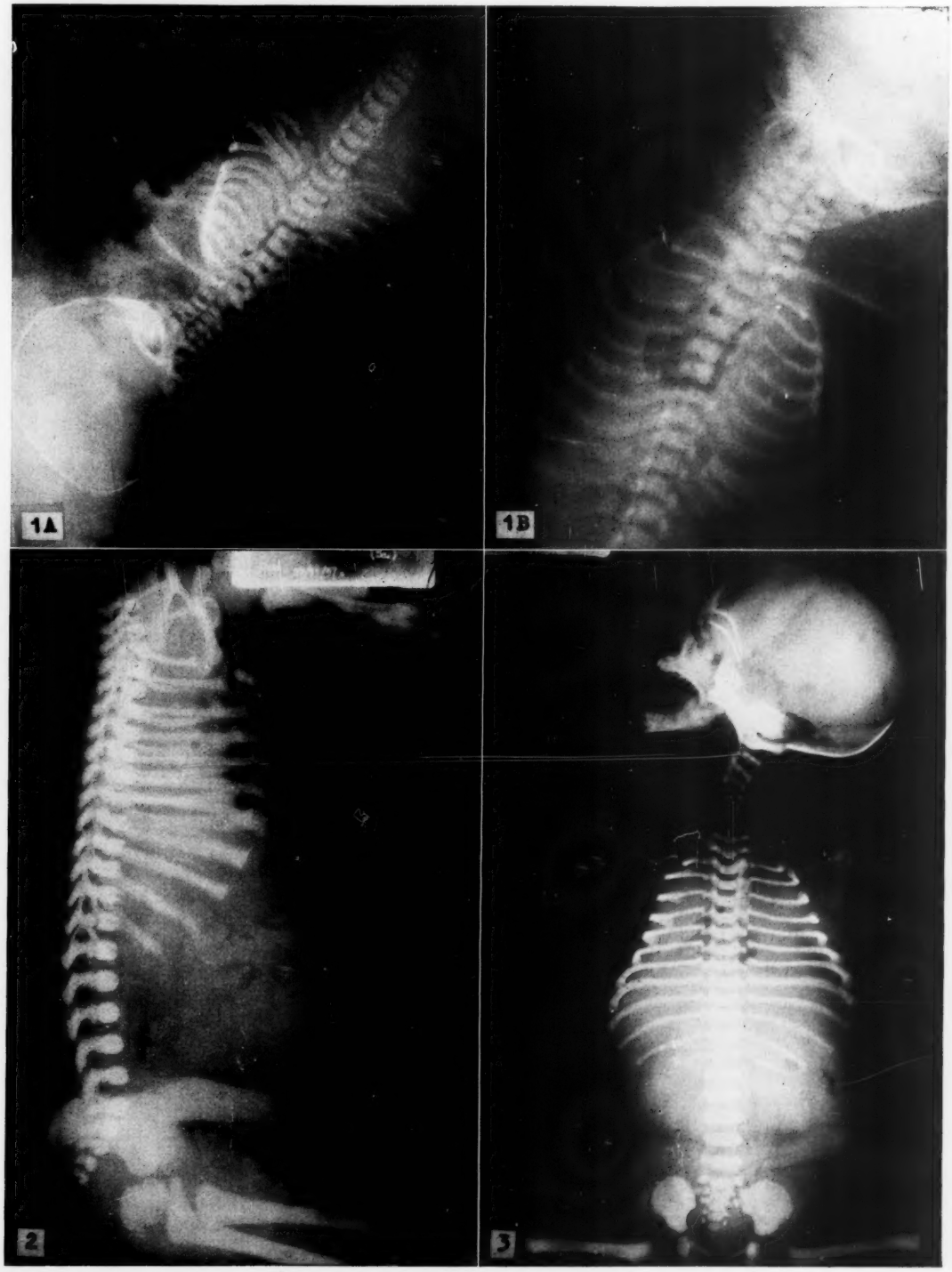

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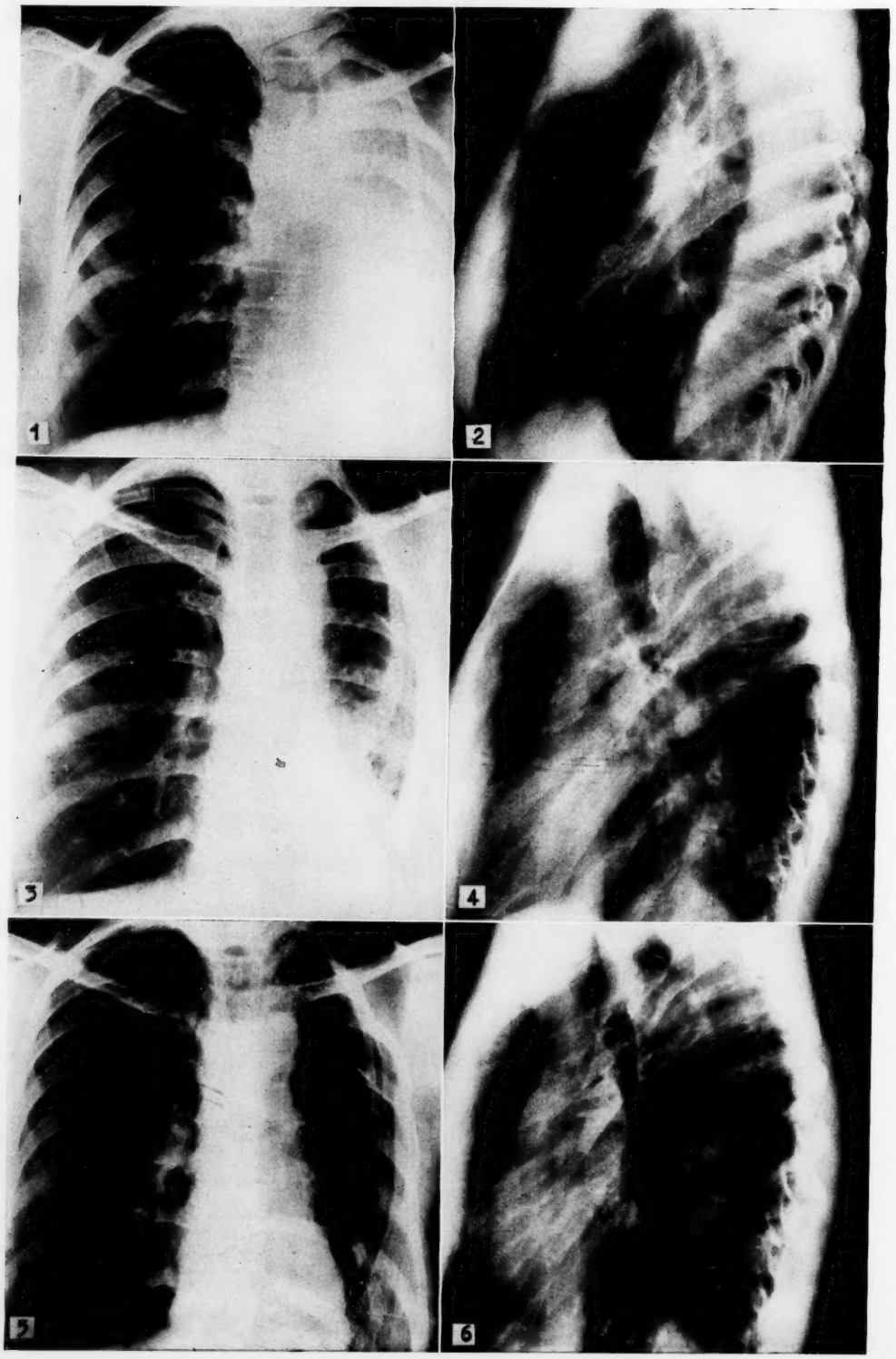

TABLE I.

The Effect of ACTH on the Urinary Excretion of 17-Ketosteroids (17-KS).

Patient Number.	Age. (Years.)	Sex.	Excretion of 17-KS. (Milligrammes per 24 Hours.)				Increase in 17-KS. (Percentage.)		
			Basal.	Day of ACTH.			Day of ACTH.		
				1	2	3	1	2	3
4	42	F.	3·8	6·5	6·1	6·0	71	61	58
5	49	F.	2·5	4·2	6·3	13·8	68	152	453
6	34	F.	6·3	12·8	16·8	18·0	103	168	170
7	30	F.	7·5	10·3	14·2	17·0	37	89	127
8	58	F.	5·4	10·9	12·7	15·9	102	135	195
9	52	F.	5·4	7·5	7·0	10·5	39	30	95
10	50	F.	0·9	2·9	2·5	3·4	222	178	278
11	50	F.	3·6	7·6	7·1	—	111	97	—
12	38	F.	2·6	3·8	4·5	—	46	73	—
13	64	F.	4·1	7·4	6·4	—	81	56	—
14[1]	26	F.	3·5	2·1	1·7	1·7	—	—	—
15	57	M.	3·2	3·3	4·4	4·8	—	—	—

[1] On cortisone (25 milligrammes daily).

was collected at three intervals; two four-hour specimens during the course of the infusion, and a 16-hour specimen for the remainder of the period. Sodium and potassium were estimated (EEL flame photometer) in the four-hour sample excreted during the latter half of the infusion and also in the entire 24-hour specimen. Steroid determinations were carried out on the 24-hour specimen.

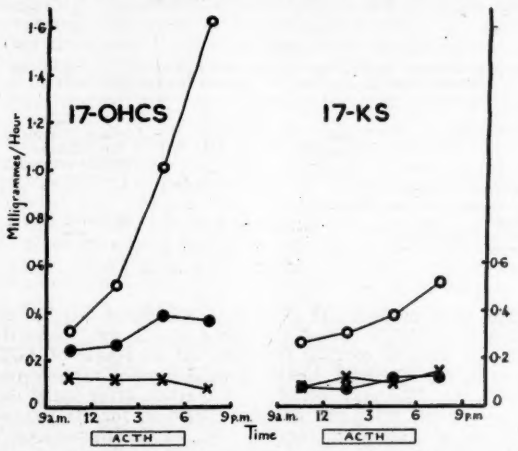

FIGURE I.

The effect of a single infusion of ACTH on the steroid content of three-hourly urine samples from three subjects suspected of having adrenal cortical insufficiency. Open circles = Case 1 (positive response to ACTH). Crosses = Case 2 (Addison's disease). Black disks = Case 3 (Addison's disease).

ACTH was obtained from the Commonwealth Serum Laboratories, Parkville, Victoria; a single batch was used for all intravenous work. At each infusion 40 units were administered in 500 millilitres of 5% glucose saline solution.

Total neutral 17-ketosteroids were determined by the Callow-Zimmermann method as modified by the Medical Research Council Committee on Endocrinology (1951). Alcoholic potassium hydroxide was stabilized with ascorbic acid (Hamburger, 1952). Recovery of dehydroepiandrosterone added to urine was in the range of 80% to 94% (five experiments); variation between complete duplicate estimations was less than 7%.

Total 17-hydroxycorticosteroids were measured by the method of Appleby, Gibson, Norymberski and Stubbs (1955), based on the estimation of 17-ketogenic steroids developed by Norymberski *et alii* (1953). The determination involved the initial removal of naturally occurring 17-ketosteroids by reduction with sodium borohydride; 17-OHCS were then selectively oxidized with sodium bismuthate to 17-KS, which were then extracted and assayed in the usual way. The normal range for males is 10 to 20 milligrammes per day and for females 5 to 13 milligrammes.

The water excretion test was carried out as described by Kepler *et alii* (1942).

Results.

Figure I shows the results of three-hourly urinary 17-KS and 17-OHCS analyses from three patients receiving ACTH for one day only; the value for each three-hour period was expressed as milligrammes of steroid per hour.

The urinary steroid levels of twelve patients, before and after two or more days of ACTH, are shown in the first two tables; Table I shows the values for 17-KS and Table II those for 17-OHCS. The percentage increase in steroid output above the control value during the days of ACTH treatment is also listed for each patient in these tables.

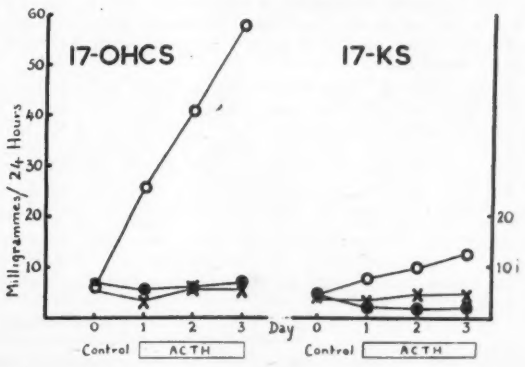

FIGURE II.

The effect of three days' intravenous administration of ACTH on the 24-hourly excretion of urinary steroids. Open circles = average values for six subjects responding to ACTH. Crosses = Case 14 (Addison's disease). Black disks = Case 15 (Addison's disease).

Some of the results in Tables I and II are shown graphically in Figure II, where a comparison is made between six patients who responded to ACTH on three successive days and two subjects of Addison's disease treated for a similar period. The average daily excretion of the six responsive patients is compared with the individual values of the two patients who were unaffected by corticotrophin.

TABLE II.

The Effect of ACTH on the Urinary Excretion of 17-Hydroxycorticosteroids (17-OHCS).

Patient Number.	Age. (Years.)	Sex.	Excretion of 17-OHCS. (Milligrammes per 24 Hours.)				Increase in 17-OHCS. (Percentage.)		
			Basal.	Day of ACTH.			Day of ACTH.		
				1	2	3	1	2	3
4	42	F.	5·8	14·8	31·0	32·2	155	443	455
5	49	F.	5·2	18·7	29·7	56·3	260	472	982
6	34	F.	6·8	38·1	64·4	85·7	460	847	1160
7	30	F.	9·7	26·2	42·8	71·3	170	321	635
8	58	F.	4·4	36·4	58·5	71·0	727	1023	1510
9	52	F.	10·9	36·7	44·7	63·0	206	310	480
10	50	F.	2·3	18·1	18·4	25·8	688	700	1002
11	50	F.	7·6	34·6	43·9	—	356	478	—
12	38	F.	2·8	10·0	14·1	—	257	404	—
13	64	F.	5·9	27·0	23·0	—	358	290	—
14[1]	26	F.	7·1	5·7	5·8	6·9	—	—	—
15	57	M.	5·3	3·1	5·3	5·2	—	—	—

[1] On cortisone (25 milligrammes daily).

Indirect evidence of adrenal function is presented in Table III. Changes in eosinophil levels and in urinary sodium/potassium ratios are shown for patients who responded to ACTH and compared with the data from the patients who did not respond. Results of the Kepler test are also listed in the table.

In Table IV some average values are given for the group of ten patients who responded to ACTH. The increment (in milligrammes per 24 hours) in the excretion of 17-OHCS after the first day of ACTH treatment is shown, together with the average change in the urinary sodium/potassium ratio over the same period.

Discussion.

All the patients in this series were investigated because they bore suggestive signs of Addison's disease.

Preliminary work was carried out on three patients by following changes in urinary constituents at three-hourly intervals, before, during and after a single six-hour infusion of ACTH. Although results were decisive in this single 12-hour test, the desirability of observing adrenal cortical response to sustained stimulation led to the work on a group of twelve patients, in which 24-hourly urine specimens were analysed after treatment with ACTH for two or more days.

In each group there were two patients who failed to respond to ACTH; the unmistakable response shown by all other patients enabled a clear distinction to be made between real and apparent cases of Addison's disease. Figure I shows that in the smaller group the steroid values in the two patients with Addison's disease were unaffected by ACTH, whereas a pronounced increase in urinary steroid output indicated definite adrenal activity in the third member of this group. Normal adrenal cortices were subsequently found in this patient at autopsy. Again, in the larger group, it can be seen from Tables I and II and Figure II that three days' treatment with ACTH caused no increase in the urinary steroid levels of the two Addisonian patients (14 and 15), in marked contrast to all other patients who were similarly tested.

TABLE IV.

Average Changes in Urinary 17-Hydroxycorticosteroids (17-OHCS) and Sodium/Potassium Ratio in Ten Patients Responding to ACTH.

Factor.	Basal Value.	Value After First Day of ACTH.	17-OHCS Average Increment and Range. (Milligrammes.)
17-OHCS (milligrammes per 24 hours)	6·1	26·1	20·0 (7·2–30·0)
Sodium / potassium ratio	3·0	1·1	—

The data in Table II show that, compared with 17-KS, urinary 17-OHCS values provide a much more sensitive index of adrenal cortical function. At all stages of ACTH stimulation, 17-OHCS levels increased more rapidly than 17-KS, the difference being most marked after three days of treatment, when the average excretion for six patients showed a 24-hourly increase of 51 milligrammes of 17-OHCS, compared with a corresponding increase of eight milligrammes for 17–KS (Figure II). Based on 17-KS excretion alone, response to ACTH was often indefinite,

TABLE III.

Indirect Evidence of Adrenal Function: Results of Kepler Test and Changes in Eosinophils and Urinary Sodium/Potassium Ratio after ACTH.

Patient Number.	Response to ACTH.	Urinary Sodium/Potassium Ratio.			Percentage Fall in Eosinophils.		Kepler Factor.
		Basal.	Eight Hours after Commencing ACTH.	Twenty-four Hours after Commencing ACTH.	After First Day of ACTH.	After Second Day of ACTH.	
1	Positive.	3·7	0·7	—	58	—	10
4	Positive.	2·5	1·5	1·6	65	93	17
5	Positive.	4·4	3·9	2·1	—	—	5
6	Positive.	2·5	0·5	0·6	90	80	Normal.
7	Positive.	2·8	1·3	1·4	100	100	Normal.
8	Positive.	2·9	1·1	1·2	50	100	Normal.
9	Positive.	2·7	—	0·8	18	60	Normal.
10	Positive.	3·2	0·4	0·5	39	85	Normal.
11	Positive.	2·7	0·3	0·9	86	88	Normal.
12	Positive.	3·5	0·8	1·0	77	87	Normal.
13	Positive.	2·3	—	0·9	94	91	Normal.
14	Negative.	2·6	3·3	3·2	22	0	—
15	Negative.	2·4	3·3	2·6	0	0	Normal.
2	Negative.	2·3	3·1	2·8	50	—	5
3	Negative.	—	—	—	46	—	—

particularly after the first day of infusion. Similar conclusions were reached by Jenkins *et alii* (1955), Engbring *et alii* (1956), and Levell *et alii* (1957), and there can be no doubt that the estimation of urinary 17-OHCS can provide valuable information in circumstances in which other procedures fail.

In the development of clinical tests for adrenal insufficiency, the significant contributions of Thorn and his co-workers reflect the search for a reliable and sensitive measurement of adrenal cortical reserve. The original corticotrophin test (Thorn, Forsham, Prunty and Hills, 1948) relied on indirect evidence of function, and the need for a direct index of adrenal activity led to the incorporation in the test of 17-KS determinations (Thorn, Forsham, Frawley, Wilson, Renold, Frederickson and Jenkins, 1951). Finally, with a reliable method for the estimation of hydrocortisone and its urinary metabolites (Porter *et alii*, 1950; Reddy, 1954), the renal excretion of 17-OHCS was found to be the most sensitive index of adrenal response to corticotrophin (Jenkins *et alii*, 1955), and this has prompted some workers to omit the estimation of 17-KS and rely solely on 17-OHCS excretion in clinical studies of adrenal function (DeFilippis and Young, 1957).

The method of 17-OHCS determination used in this paper differs completely in principle from the Porter-Silber technique, and is based upon the determination of 17-ketogenic steroids elaborated by Norymberski *et alii* (1953). The successful application of this procedure to the clinical assessment of adrenal function has been reported by several workers (Hubble, 1955; Birke, Plantin, and Diczfalusy, 1956; Wolfson, 1954; Levell *et alii*, 1957). After comparing this type of determination with the Porter-Silber technique, Moxham *et alii* (1956) concluded that the 17-ketogenic procedure was better suited for routine estimation of 17-OHCS.

Quantitative data on the renal excretion of 17-OHCS following ACTH stimulation can give decisive diagnostic aid in cases in which the usual tests for Addison's disease cannot be applied. Patient 3 (Figure I) was known to have amyloidosis superimposed on long-standing chronic nephritis and arthritis, and it was difficult to decide on clinical grounds whether progressive pigmentation (and low blood pressure) indicated adrenal involvement. Renal damage, resulting in a disturbance of water control and in excessive loss of salt, precluded the use of common tests for Addison's disease, but the failure of infused ACTH to alter markedly the urinary levels of 17-OHCS confirmed the diagnosis of adrenal insufficiency. Several months later the patient died from a pulmonary infection, and histological examination showed extensive infiltration and destruction of the adrenal cortical cells by amyloid. Renal amyloidosis was also marked. Cope *et alii* (1953) described a similar case, and in a review of the literature cited 14 examples of Addison's disease caused by adrenal amyloidosis; ACTH tests for adrenal function were not carried out, and the invariable renal involvement added to the difficulties of the diagnosis.

Unless confirmed by response to corticotrophin, misleading impressions of adrenal reserve may be drawn from the slight but definite excretion of cortical hormones that may occur even in the presence of Addison's disease (Laidlaw *et alii*, 1955). In Table II it can be seen that the basal excretion of the Addisonian patient 15 was five milligrammes of 17-OHCS per day, an appreciable value, though well below the normal range (10 to 20 milligrammes). This patient's condition would thus appear to be an example of Addison's disease due to partial adrenal failure, a condition that has been discussed in some detail by Martin, Gray, Livingstone and Lunnon (1957). The postulated origin of 17-OHCS in these patients is a remnant of functional adrenal cortical tissue which, being under constant maximal stimulation by endogenous ACTH, is unable to respond further to administered hormone. The occurrence of partial adrenal insufficiency explains how some patients with frank clinical signs of Addison's disease have been known to survive without steroid replacement therapy for periods far longer than the life expectancy associated with untreated complete adrenal failure. Adrenal crisis may develop in such patients following incidental infection or atrophy of residual cortical tissue.

Prunty (1956) used a corticotrophin test to investigate the adrenal status of a wide group of patients, and reported several patients with low basal 17-KS and 17-OHCS, who nevertheless responded sensitively to ACTH. Some of these patients showed clinical signs of Addison's disease and hypopituitarism, and in order to distinguish them Prunty chose to regard their conditions as examples of what he called "basal hypo-adrenal corticalism". Patients 10 and 12 (Tables I and II), with their low resting levels of steroid excretion and their marked response to ACTH, would appear to be aptly described by this term.

The 17-OHCS detected in the urine of patient 14 (Figure II) would have been derived largely from administered cortisone (25 milligrammes daily). The clinical symptoms of Addison's disease in this case were striking, and the unaltered excretion of 17-OHCS after three successive days of intravenous infusion with potent ACTH was taken as a further sign of adrenal cortical insufficiency. This interpretation of the results of the corticotrophin test might be questioned on the grounds that the administered cortical hormone suppressed adrenal function and prevented a response to ACTH. However, Nabarro *et alii* (1957) reported two cases in which prednisolone (20 milligrammes daily) did not prevent a response to corticotrophin, and Norymberski *et alii* (1953) described a similar finding with a patient receiving 75 milligrammes of cortisone per day. Personal observation (data not shown in this paper) of an arthritic patient on steroid therapy (12 milligrammes of prednisolone) showed that ACTH caused a pronounced increase in 17-OHCS excretion. Five patients who had been treated for several months with cortisone (50 to 70 milligrammes), and who were then placed on 9α-fluorohydrocortisone (0·5 to 1·5 milligrammes) during an ACTH test were found by DeFilippis and Young (1957) and Laidlaw *et alii* (1955) to respond to the administered corticotrophin by the third day of treatment. The evidence from these nine quoted cases suggests that treatment with physiological amounts of steroid hormones does not prevent normal adrenal cortices from responding to repeated doses of ACTH.

For an ACTH test to be of practical value in routine clinical use, it is useful to know as soon as possible whether or not there is a response to the infused hormone. In true cases of Addison's disease and pituitary failure the patients need to be tested for several days before a definite decision can be made on the status of the adrenals, whereas it is clear from the data presented here that patients with false signs of adrenal insufficiency (who seem to make up the bulk of this sort of investigation) can be easily distinguished after one day of ACTH. It is therefore desirable to know the effect of the ACTH on the first day to decide whether the infusion should be continued on the next. Steroid determinations are lengthy procedures and cannot help in this direction. Indirect evidence of stimulated adrenal function may often be rapidly obtained from the fall in the number of circulating eosinophils and from changes in the concentration of urinary sodium and potassium.

Short-term treatment of normal subjects with ACTH causes a retention of sodium and excretion of potassium (Sprague, 1951), seen most readily by a fall in the urinary sodium/potassium ratio. The changes in electrolyte balance are similar to those caused by large amounts of hydrocortisone and corticosterone (Thorn, Jenkins and Laidlaw, 1953), and it seems most likely that excessive secretion of these cortical hormones during corticotrophin stimulation (Peterson, 1957) is directly responsible for the fall in sodium/potassium ratio (Neher, 1957). Table III shows that patients who responded to ACTH (as judged by steroid excretion) exhibited an immediate drop in sodium/potassium ratio, in marked contrast to the patients who were not affected by ACTH. In ten of the eleven patients who responded, the ratio fell at least to one-half of the control value after the first day of ACTH, and in

urine collected over the latter four hours of the eight-hour infusion period the sodium-potassium ratio was similar in most cases to that in the 24-hour specimen, timed from the start of the ACTH infusion. Although the ultimate assessment of adrenal function rested on the determination of cortical hormone excretion, the analysis of urinary sodium and potassium eight hours and twenty-four hours after commencement of ACTH gave a good indication on most occasions whether the treatment should be continued for more than one day. Daily variation in salt intake and the presence of renal disease can complicate the interpretation of sodium/potassium ratios; nevertheless, the results in this small series of cases substantiated the work of Nabarro (1954) with a larger group of patients, in whom the determination of the urinary sodium/potassium ratio was found to be a most convenient screening test for ACTH response.

The results in Table II show that the excretion of 17-OHCS rose sharply when ACTH was given on successive days. For diagnostic purposes, the increase on the first day was sufficiently great to differentiate the patients who responded to ACTH—the increase being always greater than 150% of the control value. The average increment (in milligrammes) in 17-OHCS excretion for the ten patients in Table II who responded to ACTH is shown in Table IV, together with average values for the urinary sodium/potassium ratio before and after administration of ACTH. It can be seen that the average increase of 20 milligrammes of 17-OHCS after the first day of corticotrophin, accompanied by the marked fall in the sodium/potassium ratio, allowed a definite and rapid assessment to be made of adrenal cortical function.

The evidence from eosinophils was not so helpful. As a significant indication of response to ACTH, the number of circulating eosinophils at the end of an eight-hour infusion should show at least an 80% fall below the level at the start of the infusion (Bayliss, 1954). Table III shows that on the first day of administration of corticotrophin a significant fall was seen in less than half of the patients who had definite adrenal cortical reserve, the changes being more pronounced on the second day of treatment, when all but one of the patients showed a significant fall. As an early indication of the effect of ACTH, the urinary sodium/potassium ratio was found to be more reliable.

To overcome the inconvenience of intravenous procedures, several workers have developed tests using intramuscular administration of ACTH (Nabarro *et alii*, 1957; Jenkins *et alii*, 1955). The chief drawback to these developments has been the varying potency of different preparations of corticotrophin—a source of confusion that is largely avoided with intravenous methods (Ross and Thorn, 1957; Prunty, 1956). With improved grades of commercial material, greater uniformity of response may be expected from intramuscular tests, although some workers have reported occasional anomalous results with ACTH preparations of high potency (DeFilippis and Young, 1957; Streeten, Phil, Seltzer, Pont and Conn, 1955). All intravenous tests used in the present work were carried out with the same batch of ACTH.

Comparison of intravenous and intramuscular tests after three days' stimulation led Engbring *et alii* (1956) to conclude that the latter produced a greater adrenal response than the former, although it was pointed out that ACTH had been administered intravenously over six hours and a higher excretion of 17-OHCS would have been expected with an eight-hour infusion. This seems to have been borne out by the present work, since in Table II the values for 17-OHCS, estimated by a (ketogenic) procedure similar to that used by Engbring, are as high as, or higher than, the results of the intramuscular tests reported by these workers (average maximal increase in 17-OHCS found by Engbring *et alii* in 22 cases was 607%; the increase for six patients in the present series was 970%).

The risk of adverse reactions in subjecting patients with adrenal insufficiency to the stress of intravenous injections was mentioned by Martin *et alii* (1957) and Nabarro (1954). In the extensive experience of Jenkins *et alii* (1955), potentially serious reactions were rare; the few patients who reacted adversely required immediate treatment with hydrocortisone to avert the possibility of an adrenal crisis.

As may be seen in Table III, divergent results were obtained in several cases in comparing the ACTH test with the water excretion test of Kepler, Robinson and Power (1942). Low Kepler factors indicative of Addison's disease were found with three patients, who showed a definite response to ACTH; one of these patients had nephritis, but no explanation could be found for the low values in the other two patients. The list of conditions that may cause the Kepler test to give false indications of adrenal insufficiency is considerable (Bayliss, 1954), serious sodium depletion of whatever origin being a general cause of interference (Smart, 1953). On the other hand, a normal Kepler factor may be occasionally found in Addison's disease. Martin *et alii* (1957) have described such a case, and patient 15 in Table III provides another example. The occurrence of normal Kepler factors in these cases of Addison's disease, due to partial adrenal failure, is not altogether surprising, since it is feasible that the secretion of hydrocortisone by the remnant of functional cortical tissue might be just sufficient to prevent gross abnormality in the diuretic response to a water load. The value of the Kepler test seems doubtful in view of the more direct methods that have been developed for the assessment of adrenal function. A better water load test is that of Soffer and Gabrilove (1952), which depends on the reversal by cortisone of the delayed diuretic response in cases of adrenal cortical insufficiency.

Summary.

By observing the effect of ACTH on the excretion of urinary 17-hydroxycorticosteroids, it was readily possible to distinguish real from apparent cases of Addison's disease. Out of 15 suspected subjects, four were shown to have the disease.

Urinary 17-hydroxycorticosteroids provided a far more sensitive index of adrenal cortical function than urinary total neutral 17-ketosteroids, and enabled Addison's disease to be detected in rare conditions of adrenal amyloidosis and partial adrenal cortical failure.

In the subjects who responded to ACTH the increase in corticosteroid excretion after a single eight-hour infusion of the hormone was found adequate to exclude the diagnosis of Addison's disease; in subjects who did not respond the results were best confirmed by three days' treatment with corticotrophin.

The effect of ACTH on the urinary excretion of sodium and potassium provided a rapid indication whether the infusion should be continued for more than one day. In this respect changes in the urinary sodium/potassium ratio were more decisive than changes in the number of circulating eosinophils.

In several cases the ACTH test and the Kepler-Robinson-Power water excretion test gave conflicting evidence on the status of adrenal function.

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THE CERVICAL CANAL AND ABORTION.

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PATIENTS with a history of previous abortions generally do not present themselves to the clinician until again pregnant. It is only after a further abortion that pre-natal investigation is possible. Any woman who has suffered two or more consecutive abortions should have a hysterogram performed to exclude abnormalities of the uterus, not only of the body, but also of the cervical canal.

In the X-ray reports on hysterograms of the following cases, the uterine cavities were all regarded as normal in their size and contour, but no mention was made of the shadows cast by the opaque medium outlining the cervical canal. In this paper measurements are recorded of the width of the cervical canals as shown hysterographically, and these findings are correlated with the outcome of subsequent pregnancies. It is realized that the cervical measurements stated herein, although corrected for radiological magnification and foreshortening, are not as mathematically precise as in X-ray pelvimetry. However, it is believed that they are sufficiently accurate to permit of their division into two groups, the first up to six millimetres, and the second greater than six millimetres in width. In Group I patients who had corpus luteum therapy controlled by pregnanediol excretion estimations, so that decidual failure was corrected, showed an improve-

TABLE I.

The Results of Pregnancies Grouped According to Treatment and Cervical Measurement.

Management.	Group I. Width of Cervix Six Millimetres or Less.		Group II. Width of Cervix Over Six Millimetres.	
	Abortion.	Mature Fœtus.	Abortion.	Mature Fœtus.
Hormone treatment with pregnanediol control ..	2	8	4	4
No treatment (pregnanediol test performed) ..	1	0	2	0
Empirical treatment ..	3	1	4	0
Total	6	9	10	4

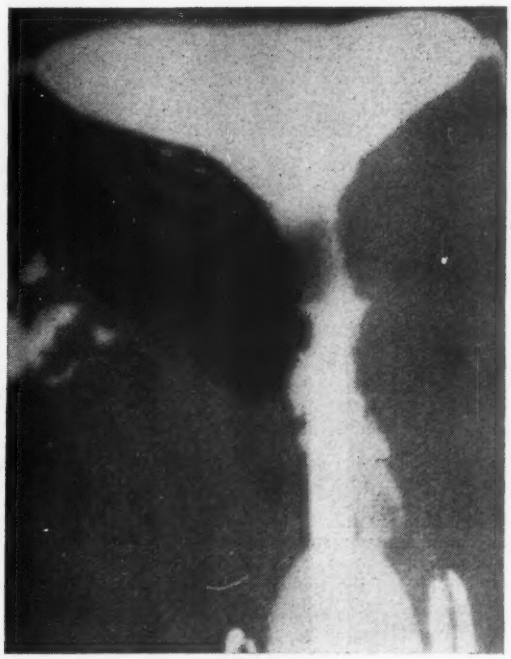

FIGURE I.
Case I: Hysterogram.

ment in the number of mature pregnancies and a decrease in the number of abortions. Four of the five patients who were untreated or who received empirical treatment aborted again. In Group II the patients treated with corpus luteum hormones regulated by pregnanediol excretion estimations had more hope of a successful pregnancy than the untreated or empirically treated ones (Table I).

FIGURE II.
Case II: Hysterogram.

In the Group I series there were 12 patients in whom 39 previous pregnancies had resulted in four mature babies. In the 15 pregnancies subsequent to the hysterograms, 11 patients were investigated by weekly pregnanediol excretion tests. One patient, who was not given hormone treatment, aborted. The other 10 patients required increasing quantities of ethisterone and/or progesterone. Their pregnancies resulted in eight mature babies and two abortions.

The following are typical examples of cases in Group I, in which it would appear that decidual failure was the important factor.

CASE I.—Mrs. A. gave a previous history of an abortion at 10 weeks in 1950, a full term baby in 1951, abortions at 12 weeks in 1953 and 1954, and at 10 weeks in 1954, after which a hysterogram was made (Figure I). In 1956 she was again pregnant and treatment under control of urinary pregnanediol estimations was commenced; the ethisterone had to be increased from 20 milligrammes a day at eight weeks to 50 milligrammes a day at 13 weeks. After a marked fall at 24 weeks the ethisterone was raised to 100 milligrammes and again at 28 weeks to 150 milligrammes a day. The dosage was gradually reduced to 50 milligrammes at 31 weeks and ceased at 34 weeks. A living female infant, weighing seven pounds four ounces, was born at 39 weeks. In 1957 this patient again became pregnant; she attended her doctor and refused to have all the "fuss and tablets of the last pregnancy". The patient again had an abortion at 12 weeks.

CASE II.—Mrs. B. gave a history of four abortions at 29, 21, 18 and 19 weeks respectively. After a hysterogram was made (Figure II) she was given weekly injections of depot progesterone, but again had an abortion at 27 weeks, even though the pregnanediol excretion, which was low at 21 weeks, had risen to above the average normal level. In this pregnancy mental agitation appeared to be the main factor, though the hysterogram shows wide dilatation of the cervix except at the actual region of the internal os.

CASE III.—Mrs. C. had aborted in previous pregnancies at 16, 18, 13 and 17 weeks. Then a skiagram was taken which was reported to show normal contour. In 1955 she had controlled corpus luteum therapy and had a living mature baby. In 1956 she had uncontrolled prophylactic treatment with 25 milligrammes of ethisterone per day, and had an abortion at 10 weeks. In 1957 she had controlled treatment with ethisterone and progesterone and had a living mature baby.

FIGURE III.
Case IV: Hysterogram.

In the second group there were 12 patients in whom 44 pregnancies prior to X-ray examination had resulted in only three mature babies. Fourteen subsequent pregnancies resulted in four mature babies and 10 abortions. Subdivision of this group produces further enlightening features: (*a*) when patients received controlled progesterone therapy four had living mature babies and four

aborted; (*b*) two patients who were tested for pregnanediol excretion, but received no treatment, both aborted; (*c*) four patients treated empirically all aborted. One patient in the last group had an abortion at 23 weeks. The fœtus showed gross abnormalities. Pre-natal seminal examination in two others showed a high proportion of abnormal forms of semen.

The following are cases illustrative of the second group.

CASE IV.—Mrs. D. had an abortion at 10 weeks in 1953, at 14 weeks in 1954, at 20 weeks in 1955, then a hysterogram was taken (Figure III). Early pregnanediol tests in a pregnancy in 1957 gave very low levels. Increasing doses of progesterone were required to raise the excretion above the critical level. At 15 weeks the patient was having 20 milligrammes of progesterone three times a week by injection and 100 milligrammes of ethisterone a day by buccal absorption. At 22 weeks she complained of uterine contractions

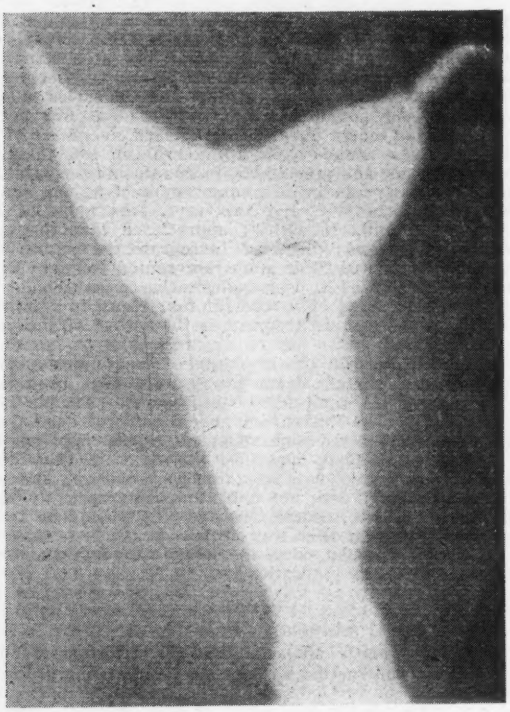

FIGURE IV.
Case V: Hysterogram.

and was given 25 milligrammes of progesterone a day until 27 weeks, when it was replaced by 200 milligrammes of ethisterone a day. At 36 weeks the internal os cervicis admitted one finger and spontaneous labour at 40 weeks resulted in a live baby weighing seven pounds 13 ounces.

In 1958 a pregnancy was satisfactory till 19 weeks; pregnanediol excretion was low in spite of 100 milligrammes of ethisterone and 25 milligrammes of progesterone a day. The tests at 24, 25 and 26 weeks showed a falling curve indicative of impending death *in utero*. Examination revealed the cervix dilated one to two fingers with membranes visible. Immediate ligation of the cervix and increased doses of progesterone (50 milligrammes) daily proved satisfactory. At 28 weeks the progesterone was decreased to 25 milligrammes a day until tests again gave low levels at 33 weeks; the cervix was still closed by the ligature, but doses of progesterone were raised to 50 milligrammes a day to obviate premature onset of labour. The patient was delivered at 40 weeks of a living baby.

CASE V.—Mrs. E. had had previous abortions in 1953 at eight weeks and 10 weeks; in 1954, when pregnanediol excretion was normal, the patient aborted twin fœtuses at 18 weeks; in 1955 she had an abortion at 17 weeks. This was followed by a hysterogram (Figure IV). She again became pregnant in 1956; the pregnanediol excretion was again higher than the average normal level without any progesterone therapy, but the patient had an abortion at 14 weeks. In this patient it is reasonable to assume that the open cervix is the major fault.

Subdivision of the present 29 pregnancies in relation to whether the patient had had primary or secondary abortions (that is after a mature pregnancy) gives further information (Table II).

The number of cases is too small for definite conclusions, but interesting trends may be noted. Thus, in the primary group with a cervical measurement of over six millimetres, nine abortions to four mature pregnancies would appear to indicate the cervix to be at fault. If this is a congenital mechanical defect, why does a mature pregnancy occur subsequent to repeated abortions? Alternately, if it is a traumatic mechanical factor subsequent to overdilation preceding curettage or occurring at delivery, why does the first abortion occur?

We must look for parallel syndromes to explain the laxity of the sphincter. Examination of the non-pregnant cervix will indicate three categories: (*a*) the number 6 dilator passes easily and painlessly through the lax, open, internal os (*b*) the number 4 dilator is painless, but

TABLE II.
The Results of Pregnancies Grouped According to Cervical Measurements and Primary and Secondary Abortions.

Cervical Measurement.	Primary.		Secondary.		Total.	
	Abortion.	Mature Fœtus.	Abortion.	Mature Fœtus.	Abortion.	Mature Fœtus.
Up to six millimetres ..	5	5	1	4	6	9
Above six millimetres ..	9	4	1	0	10	4
Total ..	14	9	2	4	16	13

numbers 5 and 6 are painful. This occurs in non-dysmenorrhœic patients in whom the stretching is accompanied by discomfort (normotonic type); (*c*) the number 4 dilator reproduces the pain of spasmodic dysmenorrhœa, and attempted passage of numbers 5 and 6 will produce severe pain. Somewhat similar conditions of spasm and atonicity may be observed by radiological examination of the sphincters in the gastro-intestinal tract.

Slow dilatation of the cervix during the first stage of labour is seldom due to structural rigidity, but is generally associated with local spasm or incoordinate uterine action and will often respond to dihydroergotamine.

The evidence suggests that laxness of the internal os uteri is not necessarily mechanical. In some cases of patulous cervix there is evidence of previous injury. However, in the majority the relaxation of the sphincter appears to be due to lack of chemical control, and the condition is aggravated by excessive Braxton Hicks uterine contractions.

Summary.

A study of the hysterograms of a small group of patients who had suffered recurrent abortions showed that with the closed cervix most cases of abortion are due to decidual failure. With the open dilated cervix the patient is very prone to abort even when the pregnanediol excretion is normal.

Acknowledgements.

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NORMAL BOWEL SOUNDS.

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> It may be possible to discover the motions of internal parts of bodies by the sound they make, that ears may discover the works performed in the several offices and shops of a man's body and thereby discover what instrument or engine is out of order. . . . I have been able to hear very plainly the beating of a man's heart and 'tis common to hear the motion of wind to and fro in the guts.

So wrote Robert Hooke (1705) 114 years before Laennec described the stethoscope. Although most modern textbooks of medicine and surgery mention the bowel sounds in connexion with the diagnosis of intestinal obstruction and general peritonitis, comparatively little attention is directed to the sounds heard from a normal abdomen. Yet one cannot form an opinion about the abnormal until the normal is fully understood.

There appear to be at least two possible methods of studying bowel sounds. One method uses expensive electronic apparatus to reduce the sound to some form of quantitative units, which may then be subjected to statistical evaluation (Farrar and Inglefinger, 1955). The other method is to accept the proposition that the study of bowel sounds is an empirical procedure, and to rely on experience to teach individual clinicians the significance of any abdominal noises heard with a stethoscope (King, 1930, 1931; James, 1934; Stevens, 1934, 1936; Vaughan and Torek, 1939; Torek, 1947; Du Plessis, 1954; Walsh, 1955).

Although at first sight it may seem desirable to follow the "scientific" approach and to reduce bowel sounds to quanta of energy, this method has two disadvantages. The equipment required is available only in large centres. Also, as will be shown, there are many uncontrollable variable factors in the production of bowel sounds. Consequently, it is necessary to have large series for comparison, and the normal range is so great that it is almost useless to apply the results to an individual case. The latter is, after all, the main interest in a study of bowel sounds.

The object of this paper is: (i) to describe a series of experiments on dogs, which attempt to elucidate some of the variable factors in the causation of bowel sounds; (ii) to describe a simple method used in listening to bowel sounds, whereby a rough quantitative assessment may be made at the bedside; (iii) to give the results of the application of this method in patients and volunteers who had no abdominal lesions.

Methods.

Animal Experiments.

Adult, healthy, mongrel bitches were used. An exteriorized loop of duodenum, or colon, was made on the ventral abdominal wall and surrounded with a tube of skin (Biebl, 1930; Douglas, 1941). In addition, one end of a fine polythene tube (bore 1·5 millimetres) was implanted into the exteriorized duodenum in the manner of a Witzel gastrostomy. The tube was passed along a subcutaneous tunnel and the other end emerged through a puncture wound in the skin on the back of the animal's neck. After the wounds had healed, in about 10 days, the animals appeared perfectly healthy and quite unaware of the tube or the exteriorized gut. It was then possible to fill the loop with fluid (water or saline), air, or a frothy mixture of water, shaken up with soap, and at the same time to observe the contractions and listen to any sounds produced. It was also possible to vary the amount of contraction in the gut by giving the animal an injection of atropine, "Banthine", or "Prostigmin" and 5-hydroxytryptamine. The method has the advantage that it is possible to listen to a short segment of intestine rather than to the whole of the abdominal contents.

Clinical Observations.

The subjects used for this study were either healthy medical student volunteers or patients in surgical wards for lesions other than those connected with the alimentary tract. The subjects lay supine and the examiner was seated comfortably. The abdomen was examined in each of the four quadrants in turn for one minute (timed with a stop watch). A diaphragm stethoscope (diameter 3·5 centimetres) was used, and it was placed approximately mid-way between the umbilicus and the anterior superior iliac spine for each of the lower quadrants, and between the umbilicus and one and a half inches below the costal margin for each of the upper quadrants. The fingers of the right hand holding the stethoscope were rested gently on the abdominal wall on each side of the diaphragm, so that any fremitus could be felt at the same time as the sounds were heard. The frequency of the sounds was charted on a line-drawing of the abdomen, and a brief note of the quality of the sounds made alongside. It was also noted in which quadrant the sounds were loudest. Many of the staccato or explosive sounds appear to come in series of a few at a time, and then there is silence for a moment before another series. These sounds were grouped together and the series counted instead of each sound separately. If the gut was active, then sounds of longer duration were heard one on top of the other. If these sounds came at intervals of less than two seconds it was not practicable to count them separately; when this occurred, the maximum count of 30 per minute was recorded as 30+, and this represents more or less continuous sound. It will be appreciated that the more frequent the sounds the more inaccurate the count. Consequently, counts of 20 or more represented frequent bowel sounds, but showed a poor quantitative measurement. If the sounds occurred only three or four times in a minute, then the count was as accurate as the record of the pulse or respiration.

In many cases the site of origin of the sounds and the distance these sounds were propagated was investigated by means of a "differential stethoscope" (Alison, 1859; Kerr, 1943). The instrument used had two end-pieces, which were connected separately, one to the right ear and the other to the left ear. The sounds were thus heard simultaneously from two points on the abdomen, and with a little practice it was not difficult to determine in which ear the sound was louder. The end-pieces could be moved separately, and in this way it was possible to find the point on the abdomen where the sound was loudest and how far the sound was transmitted.

Results.

Animal Experiments.

It was frequently observed that the exteriorized bowel was actively contracting without any sound being produced. The type of contraction, whether segmental or peristaltic, did not influence the production of bowel sound, except in so far as the tone of the gut was concerned. If the contraction forced the gut contents through or into a segment which was incompletely relaxed, then sound was produced. However, if the gut adjacent to the contracting portion was relaxed, that is had low tone, then it filled passively with the content of the contracting portion and little or no sound resulted. If five millilitres of air was injected into the loop, the contractions usually, but not always, resulted in bowel sounds which were indistinguishable from those heard in man. An injection of froth was followed by the production of similar sounds. During the injection of air or froth a series of bubbling noises could be heard and a marked fremitus felt over the exteriorized bowel. The type of noise produced in this way was similar to the explosive or crackling noises heard in man. The injection of a large volume (40 millilitres) of water into the loop produced a rushing sound while it was being injected, which was quite unlike any sound heard in man. If the contraction of the exteriorized loop was not very active, but had previously produced sounds, the complete filling of the loop with fluid was usually followed by complete silence, although the contractions continued. However, if the gut was very active, for example after an injection of "Prostigmin", then the filling of the loop with fluid did not stop the noise. The bowel sounds produced in this way differ slightly from those produced by a mixture of gas

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and fluid, in that they sound more "watery" or "sloshy". Sounds of this type are rarely heard in man, except in patients who have active gastro-intestinal bleeding. As might be anticipated, when the intestinal contractions were increased by intravenous injection of "Prostigmin" (0·25 milligramme) or 5-hydroxytryptamine (10 milligrammes per kilogram), the bowel sound increased, and when the intestinal contractions were stopped with atropine (0·6 milligramme) or "Banthine" (three milligrammes per kilogram), the bowel sound stopped.

An exteriorized loop of colon did not produce any sound which could be described as typical of colonic contractions. But occasionally short staccato popping noises, "like bubbles breaking the surface" (Cannon, 1905), could be heard even when the colon was inactive.

The frequency of duodenal contraction in the dog is 18 per minute (Douglas, 1948; Armstrong, Milton and Smith, 1956), but in no case could 18 sounds in one minute be heard, even when the gut was very active. The sound with a frequency of 18 per minute could be heard for perhaps 20 seconds, and then the remaining contractions would be silent. In other words, one cannot expect to hear the intestinal sounds every time the gut contracts, so that it is necessary to be able to recognize the rhythms of the gut over short periods.

Human Studies.

It is common experience that the loudest sounds produced in the gut may be heard from any point on the abdomen, or indeed without a stethoscope. However, not all bowel sounds are of such intensity. If 20 millilitres of air is injected as rapidly as possible down a stomach tube which is in position, the sound of the air entering the stomach may be heard from any part of the abdomen (Dudley, 1956), and also a definite fremitus can be felt in the epigastrium, but not elsewhere. The fremitus therefore localizes the site of origin of the sound better than the sound itself. In the very obese subject it may be difficult to feel the fremitus, but the sound may be heard all over the abdomen. Neither sound nor fremitus is apparent if the tube is in the œsophagus. If the volume of air which is injected down the stomach tube is reduced, then a point may be reached at which the sound of the air entering the stomach is not transmitted to all points of the abdomen. This often happens at about two to five millilitres, but individuals differ slightly in this respect; in some patients (seven out of 20) any sound produced in the stomach was heard throughout the abdomen. In this way it may be shown that a sound of this type may be produced within the abdomen and not necessarily be transmitted to all points on the surface. By performing the same test in the colon (through a colostomy) it was not found possible to produce any sound which could not be heard all over the abdomen, but any fremitus was always localized to a point superficial to the tip of the tube. The transmission of normal bowel sounds may be tested by the use of the differential stethoscope. Most of the normal sounds are heard from any point on the anterior abdominal wall; but the very quiet sounds are not transmitted more than two to three inches. These faint sounds often take the form of quiet crackling, and may be produced by "bubbles breaking the surface". When fremitus is associated with this type of noise it is usually felt in the lower abdomen, not uncommonly in the right iliac fossa. Another type of quiet sound is the usual intestinal gurgle, very much reduced in volume; it too may not be transmitted more than a few inches, and is nearly always loudest in the central lower abdomen, and any fremitus is localized to a point in this region. The large majority of all abdominal sounds are loudest in the central and lower abdomen, even if they are loud enough to be transmitted throughout the abdomen.

Farrar and Inglefinger (1955) state that subjects who have loud and frequent sounds tend to have similar sounds on subsequent examinations. Table I shows the frequency of sounds counted in eight subjects up to five hours after food on repeated examinations. It will be seen that one patient may show considerable variation from time to time (as patients 3 to 8).

The average frequency for bowel sounds heard without regard to the length of time since the last meal was 13·8 per minute. The average frequency per minute in each of the four quadrants was 12·5 in the right hypochondrium, 12·0 in the left hypochondrium, and 14·8 and 14·0 in the left and right iliac fossæ. On five occasions the frequency of the bowel sounds heard was in excess of that which was considered countable, that is the frequency count was 30+ in each quadrant. However, it is more common to hear sounds with a frequency of 30+ in one quadrant and not in the others. This does not mean that the bowel sounds were all localized to one particular region, but that the sound produced by the activity of the gut varies somewhat from minute to minute, because, as described earlier, the majority of intestinal sounds may be heard from any point on the anterior abdominal wall. On one occasion there was complete absence of bowel sounds for four minutes. The subject was a medical student who had been without food, but not fluids, for 26 hours. In 20 patients, fasted for 18 hours, bowel sounds could be heard pre-operatively, although the frequency varied from person to person. The injection of premedication ("Omnopon" one-third of a grain and atropine one-hundredth of a grain)

TABLE I.

Frequency of Bowel Sounds in Repeated Examinations.

Patient.	Average Frequency of Bowel Sounds Heard in One Minute, Within Five Hours of Taking Food.
1	26, 25, 30, 30, 21, 26, 30
2	19, 16, 30
3	17, 22, 18, 19, 4, 30, 2, 6, 8, 20, 1, 6, 6, 26, 25, 17, 16, 14
4	4, 2, 1, 4, 15, 10, 2, 10, 30, 2, 3, 7
5	2, 16, 4, 14, 4
6	2, 14, 23, 7
7	17, 17, 4
8	29, 27, 22, 12

also did not abolish the sounds in the majority of subjects examined 15 to 30 minutes after the injection, although the sounds often disappeared when the patient was placed on the operating table prior to the induction of anæsthesia. It is possible that the cause for this is the apprehension which is inevitable at such a time. The induction of anæsthesia with intravenous pentothal almost always abolishes the bowel sounds immediately. The bowel sounds may also be abolished for five to 30 minutes with an intravenous injection of "Banthine" (50 milligrammes). In people who have counts of 100 or more the effect is comparatively short-lived, whereas in those with a count of three to five per minute the abolition of the bowel sounds may last for 30 minutes.

There was no regular correlation between the length of time since the previous meal and the frequency of the bowel sounds. Some students and patients showed a steady decline in the counts from feeding up to 26 hours later; others were irregular, showing sometimes a fall in the count and sometimes no change. However, if the abdomen was examined immediately before and again within one hour after a meal, then there was a significant increase in the frequency of the sounds heard after the meal. In 20 patients the mean frequency of abdominal sounds heard in one minute was $11{\cdot}6 \pm 2$ before a meal and $16{\cdot}8 \pm 2$ after a meal. In the fasted individual the sounds tended to be fainter and higher pitched than those heard within a few hours of a meal, otherwise there did not appear to be any qualitative difference.

Very occasionally, in those in whom there is little intra-abdominal sound, a discrete bowel sound may be heard for a period of perhaps 40 seconds and its rhythm counted. The sounds which have a 20-second rhythm (once in 20 seconds) are loudest in the epigastrium, although they may be heard elsewhere; they are also associated with a fremitus which may be felt in the epigastrium but not elsewhere. This sound also has longer duration than other

sounds heard in the abdomen. The majority of abdominal sounds last for a second or two, and then they change in pitch or are overlaid by other noises. The sound with the 20-second rhythm lasts for five to eight seconds without interruption, and its pitch gets slightly higher as it proceeds, and it ends abruptly. This sound may be recognized from one person to another, but it is not common to hear it in the normal abdomen. For reasons given later it seems likely that this sound originates from the pyloric antrum and pylorus.

Another rhythm which may be recognized is one with a frequency of about 10 to 12 per minute, that is one sound every five or six seconds. In order to hear this sound it is necessary that all save a short segment of the alimentary canal shall be silent, so that the regularity of the rhythm is not masked. The quality of this rhythmic sound is the same as any other bowel sound except that the rhythm may be detected. On the two occasions on which I have heard it clearly, it was loudest in the central abdomen once and in the left iliac fossa once.

In view of the possibility that the long drawn-out sound, which was heard loudest in the epigastrium, might arise from the pyloric antrum, the time taken for a contraction to spread from the incisuria angularis to the pylorus was measured under an X-ray screen and an image amplifier. It was found that the contractions spread from the incisura to the pyloric sphincter in approximately 10 to 14 seconds.

Discussion.

The bowel sounds usually seem to be a chaotic collection of "sounds confused". The reason for this appears to be the large number of uncontrollable variable factors which are concerned in their production and auscultation. These variable factors include: (i) The majority of, but not all, sounds which occur in the abdomen may be heard from any point on its anterior surface. Consequently, sounds from the stomach, from twenty-odd feet of small bowel and from the colon, are heard superimposed on one another. (ii) Sound may be produced by any type of contraction (peristaltic or segmental). It seems unjustifiable to divide sounds into first and second degree as Du Plessis (1954) does, and to state that peristalsis occurs with the long-continued rumble, that is first degree. Peristalsis may occur without any sound at all, or may produce any type of sound, and so may segmental movements. (iii) The rhythmicity of different parts of the alimentary canal is different. The pyloric antrum in man has a rhythmicity of three contractions per minute—"the 20-second rhythm" (Carlson, 1912; Hightower and Code, 1950). The upper small intestine in man, including the duodenum, has a rhythmicity of 10 or 11 contractions per minute (Foulk *et alii*, 1954), and the terminal ileum has a slower rhythm —8·6 contractions per minute (Code *et alii*, 1957). The rhythmicity of the colon is still less, of the order of three to eight contractions per minute, but the colon of man and animals is apt to lie dormant for long periods, an hour or more, without any contraction (Adler *et alii*, 1941; Douglas and Mann, 1940; Douglas, 1941). However, even in those parts of the intestine in which contraction is regular and active, one does not hear each contraction because many occur without noise. (iv) The intestinal contents also affect the sounds, the maximum sound occurring when gas and fluid are mixed, although fluid alone, or almost alone, may cause bowel sounds if the gut is very active. This "sloshy" sound appears to occur in man when the intestine is full of blood from gastro-intestinal hæmorrhage (Milton and Clunie, 1958).

In vew of these four uncontrollable variable factors, it is not surprising that the normal range of bowel sounds is considerable. Torek (1947) and Torek and Vaughan (1939) believed that there were two factors which governed the production of intestinal sounds—the contraction of the wall and the movement of intestinal content. Walsh (1955) also believed that the contracting intestinal muscle produces sound. The movement of the contents may or may not produce sound, but the contraction of the wall is silent. James (1934) writes that the stomach produces gushing and gurgling sounds when it is full. Cannon (1902, 1911) also stated that the contractions of the pyloric antrum produced a considerable volume of sound by the regurgitation of the chyme into the stomach if the pylorus remained tightly closed. Louckes *et alii* (1952, 1953) studied the sounds which occur during the ejection of chyme from the stomach in dogs. They found that as the sound progresses it gets louder, and the pitch higher. The sound also does not last for the whole of the ejection period. Louckes thought that the change in character of the sound was probably due to the narrowing of the lumen by the contracting pylorus, which resulted in increased turbulance of the chyme.

In man it is difficult to prove that a sound originates in the pyloric region. If a sound is loudest and has a fremitus in the epigastrium, and if the sound gets louder and higher pitched as it proceeds, and also if it lasts for five to eight seconds and has a 20-second rhythm, then it is most likely to originate in the pyloric region. No other part of the gut has this rhythm and this situation. If these criteria are accepted, it is rare to hear pyloric sounds, the reason probably being that the gas and fluid content of the stomach are largely separate and that the movement of fluid alone is not as likely to produce sound.

King (1930, 1931) stated that he could hear the colon gurgling, yet gave no reason why the sounds were, in fact, colonic. In man I cannot distinguish any sound which can be definitely localized to the colon, with the possible exception of some staccato popping noises which may be associated with a fremitus in the right iliac fossa, and may therefore be caused by fluid and gas entering the caecum. Elsewhere the colon is likely to be silent most of the time, because it lies inactive for long periods (Adler *et alii*, 1941) and also the contents are more solid than in the small bowel, and presumably the movement of gas is restricted. The finding that the majority of sounds are loudest in the central and lower abdomen and that the fremitus associated with such sounds is also localized to this region suggests that the majority of bowel sounds originate in the small intestine. This is supported by the finding that when a discrete rhythm can be heard it has a frequency of about 10 per minute, which is the frequency of small intestinal contractions. James (1934), Stevens (1936, 1939) and King (1930, 1931) all state that the bowel sounds are most active after a meal, and from the animal experiments of Douglas (1948) one would expect this to be so. There is an increase in the frequency of bowel sounds if the abdomen is examined immediately before and after a meal. The variation is too great to be of value in the calculation of the normal frequency of the bowel sounds at intervals after food. Stevens (1934) considered the usual frequency of bowel sounds to be five to ten per minute; Gaussen (1952) believed it to be 10 to 12 per minute, but Torek (1947) stated that if the frequency of the sounds was less than that of respiration (20 per minute) then the sounds were diminished. The reason for this discrepancy appears to be the great variation in the normal and the difficulty of counting discrete sounds. However, in spite of the variation, it is most unusual to have a complete absence of bowel sounds in the normal abdomen for four minutes, even in a fasting subject. This finding agrees with that of Blackburn and Rob (1945). Conversely, it is not unusual to be able to hear loud and continuous sounds for up to four minutes. However, if the bowel-sound count exceeds 20 per minute in each of the four quadrants in a patient who has been without food for 12 hours or more, then the sounds may be said to be increased. The volume of sound does not indicate any pathological condition, because many normal people have very loud sounds associated with fremitus all over the abdomen.

Summary.

1. A series of observations on the production and frequency of intestinal sounds in the dog is described.

2. A method for counting the frequency of bowel sounds in man is outlined, and the results of the use of this method in normal individuals is described.

3. The findings suggest: (*a*) that the majority of bowel sounds originate in the small intestine, and (*b*) that sounds which originate from the pyloric region may occasionally be heard and that such sounds have characteristics which enable them to be recognized.

4. It is rare to have complete abdominal silence for four minutes, but not uncommon to have loud and continuous sounds in healthy individuals.

5. Increased bowel sounds are defined as a count of 20 or more sounds per minute, in each of the four quadrants of the abdomen, in a patient who has been without food for 12 to 18 hours.

6. The counting of bowel sounds is irregular when the sounds are frequent, because of the difficulty of distinguishing one sound from another. In practice, therefore, counts of less than five per minute, obtained by different observers, are comparable. If the counts are of much greater frequency an accurate comparison can be made only if the counts are all obtained by the same individual.

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THE ESTIMATION AND CLINICAL VALUE OF SERUM PROSTATIC PHOSPHATASE.

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ABUL-FADL AND KING (1949) showed that prostatic phosphatase was inhibited to 95% by 0·01M l-tartrate, which had no effect on the acid phosphatase normally present in serum. A method for the estimation of the level of serum phosphatase of prostatic origin, based on these findings, has been described by Fishman and Lerner (1953). Fishman, Bonner and Homburg (1956) reported success with the method in the diagnosis of carcinoma of the prostate and found, in this regard, that much better correlation was obtained than with the better known serum "acid" phosphatase determination.

The purpose of the present paper is to describe a slight simplification of the Fishman-Lerner technique and to record the normal and pathological ranges found by this laboratory in confirmation of these authors' findings.

Materials and Method.

The solutions required are as follows.

1. Substrate: $\frac{M}{200}$ disodium phenylphosphate.
2. Citrate buffer, pH 4·9.
3. Sodium tartrate (B.D.H. Analar), 0·2 molar solution, pH adjusted to 4·9.
4. Sodium hydroxide, 0·5 normal.
5. Sodium bicarbonate, 4·2 grammes in 100 millilitres of water.
6. 4-aminoantipyrine, 0·6 gramme in 100 millilitres of water. The product supplied by L. Light and Co. Ltd. has proved more satisfactory than that supplied by British Drug Houses.
7. Potassium ferricyanide, 2·4 grammes in 100 millilitres of water.

Two tubes are prepared as follows: Tube A, one millilitre of substrate and one millilitre of citrate buffer; Tube B, one millilitre of substrate, 0·8 millilitre of citrate buffer and 0·2 millilitre of 0·2 molar tartrate. To each tube is added 0·1 millilitre of serum, and both are incubated at 37° C. for 60 minutes. At the end of this time one millilitre of 0·5 normal sodium hydroxide is added to stop the reaction. Then one millilitre of 4·2% sodium bicarbonate and one millilitre of 0·6% 4-aminoantipyrine are added. It is essential at this point that the contents of each tube are thoroughly mixed. Finally, one millilitre of 2·4% potassium ferricyanide is added. The resulting colour which develops immediately and is stable in dim light for at least 30 minutes is read in a Spekker H760 absorptiometer with Kodak No. 4 filters. This phosphatase activity is expressed as milligrammes of phenol liberated per 100 millilitres of serum under the above-mentioned conditions (King-Armstrong units).

Serum "acid" phosphatase values were determined by the method of Kind and King (1954).

Results.

Establishment of Normal Limits.

Normal sera were obtained as fresh samples from voluntary male donors to a blood bank and estimations were made within 24 hours. Analysis of the distribution of values gave a mean of 0·06 and a standard deviation of 0·24. When mean ± 3 standard deviations were used a normal range of $0{\cdot}06 \pm 0{\cdot}72$ was obtained. Thus values of 0·8 unit or less can be regarded as normal.

Effect of Prostatic Massage.

Previous workers (King, 1955) have reported a transient rise in serum "acid" phosphatase levels after palpation of the prostate. It was thought advisable, therefore, to determine to what extent the level of prostatic phosphatase

would rise under these conditions. Eight patients were examined and a slight rise was noticed in sera obtained three to four hours after prostatic massage, with a return to the original level within 24 hours. The results are summarized in Table I.

TABLE I.
Effect of Prostatic Massage on Serum Prostatic Phosphatase Values.

Patient.	Serum Prostatic Phosphatase Values. (King-Armstrong Units.)		
	Before Massage.	Three to Four Hours After Massage.	24 Hours After Massage.
A	0·0	0·6	0·0
B	0·0	0·3	0·0
C	0·0	0·2	0·1
D	0·0	0·1	0·0
E	0·0	0·0	−0·1
F	0·2	0·8	0·4
G	0·0	0·4	0·0
H	0·0	0·0	0·3

Effect of Hæmolysis.

Heparinized blood was collected and the plasma removed. One millilitre of cells was hæmolysed with four millilitres of water and 0·4 millilitre of this cytolysate added to 0·96 millilitre of plasma. Acid and prostatic phosphatase estimations were then made on plasma, and on cytolysate *plus* plasma. The results are shown in Table II.

TABLE II.
Effect of Hæmolysis on Serum "Acid" Phosphatase and Prostatic Phosphatase Values.

Acid Phosphatase Value. (King-Armstrong Units.)		Prostatic Phosphatase Value. (King-Armstrong Units.)	
Plasma.	Plasma *plus* Hæmolysate.	Plasma.	Plasma *plus* Hæmolysate.
1·8	4·9	0·4	0·4
1·0	3·5	0·0	−0·1
0·6	3·3	0·0	0·1
3·9	6·1	0·4	0·3
1·3	4·7	0·4	0·4
3·1	6·7	0·1	0·1
3·1	8·2	0·0	−0·1
6·2	9·4	3·7	3·9
2·4	3·6	0·4	0·5

TABLE III.
Effect of Heparin on Serum "Acid" Phosphatase and Prostatic Phosphatase Values.

Acid Phosphatase Value. (King-Armstrong Units.)		Prostatic Phosphatase Value. (King-Armstrong Units.)	
Serum.	Heparinized Plasma.	Serum.	Heparinized Plasma.
1·9	1·2	0·0	−0·1
2·4	2·1	0·5	0·4
1·6	1·0	−0·1	0·0
2·7	1·5	0·2	0·3
1·8	1·6	0·2	0·2
2·7	1·8	0·1	0·3
1·1	0·6	0·1	0·0
2·5	1·7	0·0	0·0
4·9	3·9	1·3	1·3

Comparison Between Serum and Heparinized Plasma.

Table III shows estimations of both acid and prostatic phosphatase on serum and heparinized plasma. It will be noted that heparin markedly lowers the acid phosphatase value while not affecting the prostatic phosphatase value.

Correlation with Pathological Examination.

Some 300 estimations have been made in this laboratory in the past six months on patients with prostatic symptoms. Biopsy or autopsy investigations on 59 of these were performed independently and without prior knowledge of the chemical results and were kindly supplied to us by Dr. Finlay-Jones. Of 19 patients shown to have carcinoma of the prostate on histological examination, only five had normal values for serum prostatic phosphatase. Seven patients with chronic inflammation of the prostate were examined and all showed normal values. Only two out of 33 cases of benign adenoma showed values greater than 0·8. A summary of these findings is shown in Table IV.

TABLE IV.
Correlation of Chemical and Histological Findings.

Histological Finding.	Serum Prostatic Phosphatase Value. (King-Armstrong Units.)	Number of Cases.
Benign adenoma (33 cases)	<0·5	21
	0·5 to 0·8	10
	0·9 to 1·7	2
Chronic inflammation (7 cases).	<0·5	6
	0·5 to 0·8	1
Carcinoma (19 cases) ..	<0·5	4
	0·5 to 0·8	1
	0·9 to 2·0	8
	2·0 to 10·0	4
	10·0 to 200·0	2

Discussion.

The foregoing clinical correlation agrees well with the findings of Fishman, Bonner and Homburg (1956), who found that 76 out of 91 patients with proven carcinoma of the prostate had increased serum levels of prostatic phosphatase. The number of raised serum prostatic phosphatase values in cases of carcinoma of the prostate is much greater than can be obtained with the classical serum "acid" phosphatase determination. Thus these authors found that only 38 of every 100 patients with prostatic cancer had raised "acid" phosphatase values.

In cases of benign adenoma two out of 33 patients had values of prostatic phosphatase greater than 0·8. Since only biopsy material was obtainable in these two cases the presence of an undetected cancer cannot be excluded.

The danger of false positive values caused by hæmolysis is ever present in the estimation of serum "acid" phosphatase values. This has been partially overcome by the formaldehyde method of Abul-Fadl and King (1949). No such danger, however, exists in the serum prostatic phosphatase estimation.

The increase after prostatic manipulation could be a source of error. Although in the small series examined no values greater than normal were obtained, increases of up to 0·6 unit were observed. It is believed advisable that estimations should not be made for at least 24 hours after palpation of the prostate.

It is surprising to find (Table III) that the presence of heparin causes a decrease in "acid" phosphatase values. The prostatic fraction is not affected. Other anticoagulants have not yet been extensively investigated.

Summary.

A method for the determination of the prostatic fraction of serum "acid" phosphatase is described.

The findings of raised serum prostatic phosphatase levels show an exceptionally good correlation with proven cases of carcinoma of the prostate: 26% false negative values in carcinoma (19 cases); no false positives in chronic inflammation (seven cases); 6% possible false positives in benign adenoma (33 cases).

The presence of heparin or of hæmolysis does not interfere with the determination.

Prostatic massage produces a transient rise in serum prostatic phosphatase values.

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INTRAVASCULAR GAS IN THE RADIOLOGICAL DIAGNOSIS OF FŒTAL DEATH IN UTERO.

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THE diagnosis of fœtal death *in utero* can usually be suggested on clinical grounds. However, the obstetrician may fail to establish his suspicion, and most authorities agree that in any case radiographic examination is indicated for confirmation. The classical radiographic signs are well known and have been summarized by Tager (1952). In general they comprise the demonstration of the absence of fœtal life, which is of quite limited value, and the demonstration of maceration, particularly as seen in the skull and spine. In 1944 Roberts described a new sign, namely the presence of intravascular gas within the fœtus and recorded one case. The purpose of this paper is to emphasize the importance of detecting gas in the fœtal circulatory system in the radiological diagnosis of fœtal death *in utero* and to report one case in which the diagnosis was made on this basis.

This sign was not described again until 1949, when Davidson recorded two cases. Since then this finding has been reported with increasing frequency. Nash (1950) refers to two cases in a general article. Tager (1952) mentions one case in his description of a method of detecting signs of maceration, and Kettunen (1952) added another. Crick and Sims (1953) reported seven cases; Margolis and Jones (1954) two cases; Riemenschneider (1955) one case; Samuel and Gunn (1955) 15 cases; Ellenbogen, Bayer and Gottlieb (1956) one case. In 1957 Engle added two cases to the literature, and Holm, who had reported his first cases in 1954, recorded 12 cases. Lawrence (1957) described a case showing gas in the umbilical vessels only of the fœtus *in utero*, but gas was also present in the heart and abdominal cavity in radiographs of the dead fœtus taken after delivery.

Altogether 48 cases have been recorded up to the present time. Gas has been shown in the vessels of the head and neck, the heart and lungs, the abdomen, the extremities and the umbilical cord. However, the most characteristic appearances are the rounded lobulated shadows made by gas in the heart and the tree-like shadow of gas in the vessels of the liver. The common sites of gas in the dead fœtus are the heart and the vessels of the abdomen and only rarely is gas seen elsewhere when it is not demonstrable in these regions. Six of the 48 cases showed gas in the fœtal abdomen outside the circulatory system as well as within the latter. Roberts, Margolis and Jones, Crick and Sims, Ellenbogen *et alii* had one case each, and Holm described two cases.

Report of a Case.

Mrs. A., aged 37 years, was attending the ante-natal clinic of the Footscray and District Hospital, Melbourne, during the latter half of 1957 for her fifth pregnancy. She had been married six years, and her first three pregnancies in 1951 and 1952 resulted in spontaneous abortions at 10 weeks in each instance. In 1954 she was delivered of a male infant weighing eight pounds two ounces by Cæsarean section, a cervical ligation having been performed previously. During the present pregnancy she had been well, without evidence of preeclampsia. The Kahn test gave a negative result and her blood group was A Rh-positive. The expected date of delivery was December 8, 1957. In October her uterus appeared unduly large and hydramnios was suspected. A glucose tolerance test showed a fasting blood glucose of 164 milligrammes per 100 millilitres, but a return to the fasting level occurred two hours after administration of 50 grammes of glucose.

She was seen on November 21, when she stated that fœtal movements had ceased four days previously. She felt well and there were no clinical features to suggest infection. The fœtal heart was not heard. Radiological examination was performed on November 22. A single fœtus of about 38 weeks presented by the head. The uterus appeared too large for the fœtus, which showed partial extension of the limbs. There was no misalignment or overlapping of the skull bones. The upper thoracic spine showed a little accentuation of its curvature. In the lateral film of the abdomen a large collection of gas was seen within the heart; and the aorta, great vessels of the neck and upper abdominal vessels were clearly outlined (Figure I). In the antero-posterior view gas in the heart and aorta could be vaguely discerned, but the appearance in this projection would not have been pathognomonic. The diagnosis of fœtal death was made.

Severe hydramnios was diagnosed clinically, and an artificial rupture of the membranes was performed at 6 p.m. on November 26. Labour started at 9 p.m. that evening, and at 8.30 a.m. on November 27 it was evident that no advance was occurring in the second stage of labour. Forceps were applied and, with some difficulty, a dead, macerated female infant weighing 10 pounds and having a length of 23 inches was delivered. The skin was macerated, dusky red in colour and almost completely peeled off. The placenta and membranes appeared normal. Radiographs taken of the infant confirmed the presence of gas in the circulatory system, but this was smaller in amount than on the films taken of the fœtus *in utero*. Gas was now also seen in the umbilical vessels (Figures II and III).

Autopsy revealed autolysis of all the internal organs and an excess of blood-stained fluid in all the serous cavities. The skull bones were lying free and the brain was liquid.

The patient remained well and afebrile after delivery. Another glucose tolerance test was performed after three days on a diet containing 300 grammes of carbohydrate, and the findings were indicative of diabetes.

Discussion.

General.

An accurate assessment of the incidence of the radiographic signs of fœtal death *in utero* is not possible since the number of reported cases is not large enough for statistical analysis. Holm (1957), in a series of 22 cases of fœtal death which were examined radiologically before parturition, found definite signs of fœtal death in 17. In a study of the radiological diagnosis of fœtal death *in utero*, Wichtl (1955) found that 30 of 48 cases showed Spalding's sign, but in only one of these was the disalignment of the cranial bones greater than two centimetres. Pathological collapse of the spine was of little diagnostic value, and no mention was made of gas in the fœtal circulatory system. From these figures it is seen that radiographic signs of death were present in at least 65% of cases of intrauterine fœtal death. Probably if careful search is made for intravascular gas as well as for signs of maceration, in at least 75% of cases it will be possible to demonstrate evidence of fœtal death when radiographs are first requested by the obstetrician.

As with the radiographic signs in general, the number of reported cases of gas in the circulatory system of fœtuses which have died *in utero* is too small for a statistical assay of the incidence. Holm (1957) found intravascular gas after parturition in 20 of 29 fœtuses which had died *in utero* before the commencement of labour. Of these, 22 were examined radiologically during pregnancy, and the diagnosis of gas in the fœtal circulatory system was made in 12 cases. Crick and Sims (1953), in reviewing ante-partum skiagrams of 30 cases

of fœtal death *in utero*, detected gas in the fœtal circulation in 12, and the diagnosis had been made before delivery in seven cases. From these figures it seems that gas occurs in the circulatory system in at least 50% of the fœtuses which die *in utero* before the onset of labour, and that a confident diagnosis based on this sign can be made at the initial radiographic examination in at least 80% of those which prove to have intravascular gas, that is in 40% of all cases of fœtal death *in utero*.

The presence of gas in the fœtal circulation is an absolutely certain indication of fœtal death. There has been no report of a false diagnosis of fœtal death *in utero* based on this sign. Fœtal intravascular gas has to be differentiated from maternal gas shadows, fœtal fat lines and intrauterine gas, as has been emphasized by Samuel and Gunn (1955), but this rarely presents any difficulty. Out of Holm's series of 22 cases of intrauterine death in which X-ray examination was made before parturition, in 10 other signs of fœtal death were present, an incidence about equal to the finding of fœtal intravascular gas. In Wichtl's series, as we have seen, signs of maceration were present in 30 of 48 cases of fœtal death *in utero*. The accuracy of Spalding's sign has been cast in doubt. Overlapping of the skull bones has been noted in a living fœtus by De Lee (1938) and also by Thoms (1940). Milne (1939) has reported a case in which a live infant was delivered after a radiological diagnosis of intrauterine death based on signs of maceration. Billing (1941) has demonstrated that small vertical changes may result in apparently large overlapping in the radiograph. One can thus agree with Fahmy (1938) that Spalding's sign is open to considerable criticism. It would seem, then, that although the incidence of signs of maceration in Wichtl's series was somewhat higher (63%) than the incidence of gas in the circulatory system of the dead fœtus *in utero*, the difference is probably not significant when all doubtful cases are eliminated.

In over 50% of the reported cases of gas in the fœtal circulatory system this was the only definite sign of intrauterine fœtal death. The only assessment of the relative value of the sign of intravascular gas as compared with signs of maceration in the radiological diagnosis of fœtal death *in utero* has been made by Holm (1957). He found that out of 17 cases in which this diagnosis could be made from the radiographic appearances, in seven cases the films showed intravascular gas only, in five cases the films showed signs of maceration only, and in five cases both intravascular gas and signs of maceration were present. These figures are consistent with the assumption that the two features are independent variables and that each has an incidence of approximately 50%. It is noteworthy that in Holm's series the radiological diagnosis of fœtal death would have been missed in approximately two-fifths of the cases if the sign of intravascular gas had been neglected. These reports may be summarized by saying that, out of a total of 49 recorded cases of gas in the fœtal circulatory system (including the author's case), in 27 intravascular gas was the only definite sign of fœtal death, and in the remaining 22 signs of maceration were also present.

Time Relationships.

In 19 of the 49 reported cases radiological examination is stated to have been performed within seven days of fœtal death, and in 14 of these intravascular gas was the only definite sign of fœtal death, while in only five were signs of maceration also present. In nine of these 19 cases an X-ray examination was made on the third day after fœtal death and in none of these was any other definite sign of fœtal death present.

Only two cases have been reported (Samuel and Gunn, 1955; Davidson, 1949) in which the initial radiograph after fœtal death showed no abnormality and subsequent films showed gas in the fœtal circulation. In the case described by Samuel and Gunn the probable time of fœtal death is stated and the initial radiographs were taken about 48 hours later, while the subsequent films were taken eight days later. The time relationships are not stated in Davidson's case.

Two cases have been described in which the initial radiographs showed gas, and no gas could be detected at subsequent examinations (Samuel and Gunn, Crick and Sims) performed four weeks and more than two weeks after fœtal death respectively. Several cases have been reported in which the amount of gas decreased after its original radiographic demonstration. Thus it seems that in those cases in which fœtal intravascular gas can be detected *in utero* this will usually appear about three or four days after fœtal death and will remain demonstrable for at least two weeks and probably for longer periods.

Zuppinger (1954) states that signs of maceration are not seen within four days of fœtal death and usually not until after a week has elapsed. It appears, then, that fœtal intravascular gas is usually the earliest radiographic sign of fœtal death. However, no report has been published in the literature describing the detection of this sign within 48 hours of fœtal death.

Radiographic Technique.

No case has been reported in which the fœtal intravascular gas was seen in the antero-posterior view of the maternal abdomen, but not in the lateral projection. On the contrary, there have been many cases in which the appearances were pathognomonic in the lateral projection, but indefinite or apparently normal in the antero-posterior view. Thus it is necessary to obtain radiographs both in the antero-posterior and in the lateral projection in every case in which fœtal death *in utero* is suspected. The lateral film is better taken with the patient erect, as this may show a fluid level in the fœtal heart, confirming the diagnosis of intravascular gas. Tager (1952) has also shown that collapse of the spine of the dead fœtus may be seen in the erect view, even though this is not apparent on radiographs taken in the recumbent position, and although he mentions only antero-posterior projections, this sign may be seen equally well in the lateral projection. After the two routine films have been viewed, it may occasionally be necessary to take additional films as indicated.

Origin of the Gas.

Five theories have been propounded to explain the origin of the gas. Davidson thought that it was due to decomposition of blood elements. Kettunen was of the opinion that Rh immunization of the mother is a significant factor. However, of the 24 reported cases in the literature in which the maternal Rh group is stated, 19 were Rh-positive, while only six were Rh-negative. It is probable that Rh immunization of the mother was not present in those cases in which no mention was made of the Rh group. Thus it seems unlikely that this is a factor. Samuel and Gunn postulated that under certain circumstances an alteration in the physiological function of the placenta may result in gas being passed by a differential pressure gradient from the maternal into the fœtal circulation, thus producing a gas embolus which is the actual cause of fœtal death. This theory is based largely on the finding in five cases in their series of a large quantity of gas in the umbilical cord on the initial radiographs, while a smaller volume of gas was found in this region on films taken at a later time. However, it is now known that usually the volume of gas in the fœtal circulation also decreases as time passes. Moreover, this theory does not explain those cases in which the initial films after fœtal death show no gas, and this is found on radiographs taken subsequently. Margolis and Jones suggested that a maternal bacteræmia of a gas-producing organism occurs, and that the bacteria pass through the placenta to create fœtal septicæmia and death with the agonal production of gas. They found gas-producing bacteria in cultures of cord blood in their two cases, but the blood from the fœtal heart was sterile. However, Crick and Sims found that the blood samples in their cases were usually sterile, and the few instances of positive culture could be explained as being due to contamination. In the majority of the reported cases there has been no clinical evidence of maternal infection, but it has been shown by Butler that saprophytic bacteria

may be present in the maternal circulation in the absence of clinical signs of infection; and De Lee (1916) and Browne and Kincaid (1926) have reported fœtal infection while the mother has remained well. Holm (1956) expressed the opinion that the gas may originate from the liberation of chemically-bound oxygen and carbon dioxide, which occurs when hæmoglobin undergoes decomposition. This theory is supported by the finding of 60% to 65% oxygen and/or carbon dioxide in the one case in his series in which gas was collected for analysis. Crick and Sims obtained samples of the fœtal intravascular gas in five of their cases and found that it was almost wholly nitrogen. This finding cannot be explained on the basis of any of the theories which have been put forward, and further investigation of the composition of the gas in the fœtal circulatory system is required. In the present state of knowledge the origin of the gas is uncertain.

Summary.

1. Radiographic signs of fœtal death *in utero* comprise evidence of fœtal maceration and gas in the fœtal circulatory system.

2. Of all cases of fœtal death *in utero*, 65% to 75% will exhibit radiographic signs when radiological examination is first requested.

3. The radiographic signs do not appear within the first 48 hours after fœtal death.

4. Evidence has now accumulated to suggest that gas in the fœtal circulatory system is the most important radiographic sign of death *in utero*. This is based on the following considerations. (*a*) Its presence in the fœtal circulation is an absolutely certain indication of fœtal death. (*b*) It can be unequivocally detected by radiographic examination before the onset of labour in at least 80% of the cases in which it is present. (*c*) It occurs about as frequently in cases of fœtal death *in utero* as definite signs of maceration, that is each occurs in about 50% of all cases, probably independently of the other. (*d*) It usually appears earlier than the signs of maceration, often about three or four days after fœtal death.

5. The origin of the gas is unknown.

6. It is recommended that a recumbent antero-posterior view and an erect lateral view be taken routinely in all cases of suspected fœtal death *in utero*. Occasionally further radiographs may then need to be taken as indicated.

Acknowledgement.

The writer is indebted to Mr. I. A. McDonald, of Melbourne, for access to the clinical notes.

Addendum.

Since submitting this paper for publication the writer's attention has been drawn to another case of intrauterine fœtal death showing gas in the heart and aorta, Spalding's sign and collapse of the spine, two weeks after the cessation of fœtal movement. The mother, aged 28 years, had had six children and was Rh-negative. The last two offspring had died of erythroblastosis fœtalis.

Holm (1957) has produced further evidence to support his contention that the gas is derived from the decomposition of hæmoglobin. He has found another six cases which demonstrated intravascular gas in the dead fœtus *in utero*. This now makes a total of 56 reported cases.

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Legends to Illustrations.

FIGURE IA.—Lateral view, *ante partum*. Gas is demonstrated in the heart, the great vessels of the neck, the aorta and the vessels of the upper abdomen. The fœtal fatty tissue gives well-defined shadows. The skull appears normal.

FIGURE IB.—Enlarged and inverted view.

FIGURE II.—Lateral view of dead infant after delivery, showing gas in the heart, abdominal and umbilical vessels.

FIGURE III.—Antero-posterior view of dead infant after delivery, showing gas in the heart, aorta, abdominal and umbilical vessels. This is smaller in amount than on the ante-partum radiographs. The appearance of the cervical spine is due to trauma incidental to delivery of the dead fœtus.

Reports of Cases.

RECURRENT PULMONARY ATELECTASIS IN AN ASTHMATIC SUBJECT, RELIEVED BY ACUTE BRONCHITIS.

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ACUTE pulmonary atelectasis is commonly attributable to bronchial obstruction by a mucous plug, and it occurs most frequently after major upper abdominal operations. It is also encountered in poliomyelitis and tetanus patients with respiratory paralysis. The obstructing mucous plugs may be large and non-adherent to the walls of the bronchus and readily removed by postural percussion or bronchoscopy; less commonly the initial plug may be followed by a succession of plugs either in the same bronchus or in other bronchi. This latter situation is usually associated with the presence of tenacious mucus in patients suffering from asthma or chronic bronchitis. In the case here described, there were rapidly recurring episodes of bronchial obstruction, which were only very temporarily

relieved by bronchoscopy and largely unaffected by nebulized proteolytic substances, and which finally cleared after an acute bronchial infection.

Clinical Record.

The patient was a female, aged 49 years. She had had bronchial asthma of mild severity since the age of 14 years. An X-ray picture of the chest in December, 1949, was clear. In April, 1950, she had an attack of acute bronchitis and since then had been more prone than usual to colds and coughing fits. In October, 1950, a skiagram of the chest showed an opacity in the left lung; the Mantoux test gave a negative result and sputum examination revealed no tubercle bacilli. In July, 1951, she was admitted to the Royal Melbourne Hospital with the clinical and radiological picture of chronic left upper lobe collapse. At bronchoscopy, pus was seen coming from the orifice of the left upper lobe bronchus. Left upper lobectomy and left upper thoracoplasty were performed by Mr. Ian McConchie. The specimen showed a completely collapsed lobe except for a small portion of the apical segment; all the bronchi were dilated and there were abscess cavities in the lingula and in the anterior segment. There was no histological evidence of tuberculosis or carcinoma. A wound infection developed which resulted in the formation of a chronic sinus; this cleared after two years, after the discharge of a bone sequestrum.

She then remained well until February, 1956, when she attended the Thoracic Surgical Clinic of the Royal Melbourne Hospital with a history of increased amount of sputum, mostly mucoid and colourless, but occasionally thick and yellow, over the preceding month. There were now clinical and radiological signs of collapse of the left lower lobe (Figures I and II). She was admitted to this hospital on March 2, with a temperature of 99·8° F. Bronchoscopy showed the basal left lower lobe and apical lower lobe bronchi to be tightly packed with thick mucoid sputum. This sputum, at this and subsequent bronchoscopies, was too thick to be sucked out; it had to be extracted with forceps. On culture the sputum grew *Streptococcus fæcalis* and *Neisseria catarrhalis*. Crystalline penicillin, 500,000 units four times a day, was given for nine days. Since the physical signs in the chest did not alter after the bronchoscopy, a tracheal catheter was passed and the patient expectorated a large bronchial cast. However, the physical signs again did not improve; and a further film showed persistent collapse. On March 20 the sputum grew *Bacillus coli*, and penicillin and streptomycin (one gramme a day) were given for 10 days. After the expectoration of purulent sputum, the lower lobe did clear and remained expanded for 10 days; then the block recurred and three further bronchoscopies were required, at the last of which bronchial lavage was performed with warm saturated sodium bicarbonate solution, which produced numerous bronchial casts. These casts were examined histologically and showed sheets of necrotic cells surrounded by strands of mucus. The casts were also incubated with equivalent amounts of trypsin, "Hyalase" and "Varidase" (streptokinase *plus* streptodornase): trypsin was the most effective of these agents *in vitro* in dissolving the casts. On March 27 the administration of aerosol trypsin was commenced, using oxygen under pressure as the nebulizing force; the solution used contained 50 milligrammes of crystalline penicillin per millilitre in "Trypure Novo" (Evans), which is a solution of trypsin in Sorensen's phosphate buffer solution. On the first day 50,000 units (equivalent to eight milligrammes) were used, 75,000 units on the second day and 125,000 units on the third and subsequent days. There was some initial improvement, but the lobe again collapsed and two further bronchoscopic examinations were necessary. Tetracycline, 250 milligrammes four times a day, was given from April 11 to 23. With further trypsin aerosol medication, the lung remained expanded for eight days before collapsing again. On May 3, the patient developed fever, with a temperature of 101·3° F., and the production of purulent sputum. This superadded infection cleared rapidly; with it the signs of collapse of the left lower lobe also cleared, with no further recurrence (Figures III to VI). She was discharged home on May 19. At no stage during her stay in hospital was her asthma severe. When seen subsequently as an out-patient, she has remained well despite continued production of sputum, both purulent and mucoid, associated with her bronchial asthma.

Discussion.

Lobular pulmonary atelectasis in asthmatic subjects is common, particularly in children; it often clears spontaneously, and if treatment is required, it is quickly effective. Lobar collapse, such as herein described, is less frequent. Whole lung collapse is rare. Luke (1956) gives a comprehensive account of this type and suggests that obstruction of many smaller calibre bronchi is possibly a more likely factor in the collapse than obstruction of a main bronchus with its stout cartilaginous supports. However, in our patient there was clear evidence of both major and segmental bronchial obstruction.

Although bronchoscopic aspiration of the obstructing plug, together with physiotherapy, is generally the accepted management, Kinnier Wilson and Stevenson (1957) do not favour its use in their patients with respiratory muscle paralysis after poliomyelitis. They believe bronchoscopy in the presence of active bronchitis may actually be harmful. Forbes (1958), in his experiences with similar poliomyelitis cases at the Fairfield Hospital, Melbourne, did not encounter troublesome bronchitis with any such frequency and therefore had little occasion to use the proteolytic agents to be discussed. He attributed the low incidence of respiratory problems to the relatively few tracheotomies performed.

The use of aerosol trypsin proved disappointing. Trypsin is chiefly a fibrinolysin rather than a mucinase. Amongst the now numerous contributions to the literature on this enzyme, Unger and Unger (1953) reported favourably on its effectiveness in dissolving the mucoid sputum of the chronic bronchitic subject. Kofman *et alii* (1954*a*) stated that after trypsin therapy sputum viscosity was definitely reduced, although the volume of sputum was not altered. This reduction in sputum viscosity was not confirmed by Forbes and Wise (1957). Kofman *et alii* and Steigman and Scott (1952) reported lessened pulmonary complications in poliomyelitis patients who received aerosol trypsin administered in the usual way or per tracheotomy tube. However, Kofman *et alii* emphasize that trypsin is only reliably effective when it is given directly into the bronchial tree at the site of obstruction. Camarata *et alii* (1956) give a comprehensive account of their successes in atelectasis both associated and unassociated with poliomyelitis; and they stress the need for frequent aspirations of the increased bronchial secretions and also the need for antibiotic therapy for both the upper and the lower respiratory tract infections. Peck and Levin (1952) recommend that trypsin should not be used when there is active inflammation of the bronchial mucosa. Prince *et alii* (1954) suggest that in bronchial asthma the enzyme should be reserved for cases in which infection is prominent.

In some series of cases there is a high incidence of toxic effects, e.g., 53% in Kofman's (1954*b*) patients. The chief of these is a burning sensation in the tracheo-bronchial tree, leading to bouts of coughing, dyspnœa, cyanosis, hoarseness and fever. Farber *et alii* (1954) have noted histological changes in the bronchial mucosa after trypsin therapy, which they consider to be premalignant. However, these changes are not confirmed by Habeeb *et alii* (1954), who could find no evidence of metaplasia in sputum cells or in the cells of the bronchial mucosa of resected specimens.

Of the other agents used in attempting dissolution of obstructing endobronchial plugs, "Alevaire" (Bayer) has been extensively tested. "Alevaire" contains a non-toxic detergent (Triton W.R. 1339) in an aqueous solution of 2% sodium bicarbonate and 5% glycerine. Miller *et alii* (1954) reported favourably on this agent in various types of bronchial obstruction. However, Palmer (1957), using sputum viscosity as well as clinical state as a criterion of

successful therapy, found no significant difference between "Alevaire" aerosol and a simple water aerosol. Forbes and Wise (1957) also found no reduction in sputum viscosity with "Alevaire" therapy.

Streptokinase (fibrinolytic) and streptodornase (a desoxyribonuclease) are often used together. Like trypsin, they reduce viscosity of sputum, but actually increase its volume. They were not used in the present case because of their ineffectiveness *in vitro*. Farber *et alii* (1957) review the use of enzymatic therapy in diseases of the chest and conclude that such therapy, although of undoubted value in certain cases, must be used circumspectly.

In the case here reported, repeated bronchoscopies and the use of proteolytic substances proved ineffective in relieving the obstruction of the left lower lobe. It would appear that the ultimate attack of acute bronchitis with fever and purulent sputum led to the dissolution of the obstructing mucus by the production of its own proteolytic substances.

The importance to this patient of the final resolution of the series of obstructions to the left lower lobe bronchus is very clear, since the chronic collapse of the left upper lobe, and the development there of infected bronchiectasis requiring lobectomy, was doubtless attributable to a process similar to that which later affected the lower lobe.

Summary.

A case is reported of recurrent lower lobe atelectasis in a middle-aged female asthmatic patient who had previously undergone left upper lobectomy for chronic collapse with bronchiectasis.

Despite repeated bronchoscopic aspirations of the obstructing mucoid sputum plugs, physiotherapy, chemotherapy and aerosol solvents, the obstructive atelectasis recurred over a period of nine weeks, until a fresh attack of infective bronchitis led to the permanent clearing of the obstruction.

The literature pertaining to pulmonary atelectasis is briefly reviewed, with particular reference to the use of proteolytic aerosols in the management of such cases.

Acknowledgements.

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Legends to Illustrations.

FIGURES I AND II.—Postero-anterior and left lateral films of the chest, showing complete collapse of the left lower lobe (February 28, 1956).

FIGURES III AND IV.—Postero-anterior and left lateral films, showing partial reexpansion of the collapsed left lower lobe (May 5).

FIGURES V AND VI.—Postero-anterior and left lateral films, showing complete reexpansion of the collapsed left lower lobe (May 8).

Reviews.

Textbook of British Surgery. Edited by Sir Henry Souttar, C.B.E., D.M., F.R.C.S., and J. C. Goligher, Ch.M., F.R.C.S.; Volume III; 1958. London: William Heinemann (Medical Books), Limited. 9¾" × 7", pp. 628, with 207 illustrations and two tables. Price: 105s. (English).

THE third volume of the "Textbook of British Surgery" covers genito-urinary surgery, peripheral vascular diseases, plastic surgery, actinomycosis, surgery in the tropics, venereal and allied diseases, radiology and radiotherapy, surgery of the adrenal and parathyroid glands, blood transfusion, fluids and electrolytes, hæmorrhage and chemotherapy. The editors have been assisted by 15 contributors, all of whom are internationally known for their work in their particular specialty. The editors have pointed out that, whilst the advantages of surgery in the last twenty years have been so great that no one individual can master all the fields which have been opened, on the other hand it is important that candidates for the higher examinations should be familiar with the whole subject. This text-book has endeavoured to fulfil these requirements, and any candidate for a higher degree who has mastered these volumes will have no difficulty with the theoretical aspect of any higher surgical examination throughout the world.

This book reaches the same high standard as in the first two volumes, both from the point of view of authorship and also from that of publication. The production is a great credit to the publishers and the illustrations are of the same high standard as in the previous two volumes. Volume IV is still to be published and will then complete the text-book.

The Clinical Application of Hormone Assay. By John A. Loraine, M.B., Ph.D. (Ed.), M.R.C.P. (Ed.), with a foreword by J. H. Gaddum, Sc.D., F.R.S.; 1958. Edinburgh and London: E. and S. Livingstone, Limited. 8½" × 5½", pp. 380, with 66 illustrations. Price: 30s. (English).

OVER the last ten years or so very great strides have been made in the development of methods for the estimation of hormones. At first it was shown that the diagnosis of pregnancy could be achieved by simple tests in animals, depending upon the presence of large amounts of gonadotrophins in urine at that time. Such tests could be simple in the extreme, since the hormonic content of the urine in pregnancy is vastly different from that normally found. The author of this book describes methods for the estimation of a variety of hormones in the human subject. After a discussion of the general principles of hormone assay work, detailed methods are described for the pituitary gonadotrophins, chorionic gonadotrophins, thyrotrophin, adrenocorticotrophin, the growth hormone prolactin, ADH, œstrogens, progesterone, corticosteroids, 17-ketosteroids, androgens, adrenaline and nor-adrenaline, and finally insulin.

The methods described are both chemical and biological, the former having made great progress since the advent of paper chromatography. Unlike early pregnancy tests, the methods used for estimations of this kind are rarely simple,

and Professor Gaddum, in a foreword to this book, makes a plea for the rational use of such tests in integrated and fruitful research and not as isolated observations in interesting cases, where the great expenditure of time and money is put to so little use.

The author discusses with each hormone the diagnostic significance of the assay values obtained and their use in clinical medicine.

This is a book for every clinical endocrinologist. Even a brief perusal will convince the less specialized clinician that modern hormone assay techniques constitute a very special field, which owes much to the work of Dr. Loraine and his colleagues at the Clinical Endocrinology Research Unit in the University of Edinburgh.

A Comprehensive Dictionary of Psychological and Psychoanalytical Terms: A Guide to Usage. By Horace B. English and Ava Champney English; 1958. New York, London, Toronto: Longmans, Green and Company. 8¼" × 5¼", pp. 608. Price: $8.00 (text), $10.75 (trade).

THE aim of the authors in this book, which they describe as a collection of meanings rather than an encyclopædia, is to facilitate clarity and correctness in communication and to discourage careless and inexact use of terms. For example, "differentiate" is defined as "to make to differ" rather than "to distinguish", a use which the authors regard as "occasionally confusing". Many of the terms included refer to special sense physiology—e.g., fruity, hircine and luminosity, the last occupying half a page. Lynching may be bourbon (to punish an individual for a specific offence) or proletariat, when an out-group is persecuted. Psychiatric terms are defined according to the nomenclature adopted in 1950 by the American Psychiatric Association. Paraphrenia is "obsolescent" for dementia præcox and/or paranoia, but on turning up dementia præcox we are referred to schizophrenia. Psychoceramic means "crack-pot", not therapeutic pottery work. Psychosomatic medicine "emphasizes the role of psychic factors in many (or all) diseases, or in maintaining health".

Schools and divisions of psychology are tabulated on four pages. The M'Naghten rules of criminal responsibility are retained as the main test in U.S.A.; the authors do not mention the Durham test, which has recently been adopted by some States. The dictionary includes a number of neurological terms.

This scholarly work is designed primarily for psychologists, social workers, educationalists and others in related fields. Psychiatrists, few of whom, according to the authors, "have background preparation in the science of human behaviour", can make good their deficiency by reference to this book.

Forensic Medicine. By Keith Simpson, M.D.; Third Edition; 1958. London: Edward Arnold (Publishers), Limited. 8¼" × 5", pp. 360, with 137 illustrations. Price: 30s. (English).

THE third edition of this book maintains the author's design to provide a brief and practical guide to the subject. The first edition in 1947 was welcomed for its clear and concise presentation and its excellent production. The new edition has these same features, making it an interesting and attractive book for the student, and a useful one for the practitioner seeking a book for quick reference or assistance in preparing for the occasional autopsy. It gives a good cover of the everyday problems in medico-legal work, such as firearm wounds, carbon monoxide poisoning, various aspects of the alcohol question, asphyxial deaths and sex offences. The chapter on identification presents all the salient facts of a very extensive subject in a lucid and interesting manner. The various types of injuries and wounds of various regions, blood stains and blood groups are dealt with in a practical manner, and the chapters on abortion and infanticide are again excellent. There are sections on the medico-legal autopsy, evidence in courts and legal procedures, the law being that of England and Scotland. Medical ethics is dealt with briefly. The section on toxicology has been altered in some respects to include a number of new drugs which have, in recent years, become more prominent in accidental and suicidal poisoning.

Credit must be given for the excellent illustrations. Some of those in the previous editions have been replaced by more suitable ones, and the present extensive selection emphasizes very well the more important matters in the text.

This book can be recommended for the student or for the practitioner who wishes to have the essentials of forensic medicine presented in a compact form, but the practitioner doing medico-legal work regularly will probably find it too concise.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Blood Groups in Man", by R. R. Race, Ph.D., M.R.C.S., F.R.S., and Ruth Sanger, Ph.D., B.Sc.; Third Edition; 1958. Oxford: Blackwell Scientific Publications. 8¾" × 5½", pp. 400. Price: 42s. (English).

Fully revised since the previous edition appeared in 1954.

"New Biology", edited by M. L. Johnson, Michael Abercrombie and G. E. Fogg; No. 26; 1958. Victoria: Penguin Books Proprietary, Limited. 7" × 4", pp. 128, with illustrations. Price: 4s.

Contains seven articles on recent aspects of biology.

"Diseases of the Liver and Biliary System", by Sheila Sherlock, M.D., F.R.C.P., M.R.C.P.; Second Edition; 1958. Oxford: Blackwell Scientific Publications. 8¾" × 5", pp. 736, with 213 illustrations. Price: 57s. 6d. (English).

A fully revised edition, with much new material.

"IV Congreso Venezolano de Cirugia (Trabajos Libres)"; Volume II; 1957. Caracas: Prensa Medica Venezolana. 9" × 6¼", pp. 570-1028, with illustrations. Price not stated.

The second volume of proceedings of the fourth Venezuelan Surgical Congress. It is entirely in Spanish.

"Clinical Obstetrics and Gynecology", Volume I, Number 2: "Toxemias of Pregnancy", edited by Louis M. Hellman, M.D.: "Fibromyomas of the Uterus", edited by Robert A. Kimbrough, M.D.; 1958. New York: Paul B. Hoeber, Inc. 9¼" × 5¾", pp. 544, with many illustrations. Price not stated.

The second issue in this new quarterly series.

"Lectures on the Scientific Basis of Medicine", British Postgraduate Medical Federation, Volume 6, 1956-57; 1958. London: The Athlone Press. 8¼" × 5", pp. 406, with many illustrations. Price: 45s. (English).

This sixth annual volume contains 21 of the 29 lectures delivered during the winter of 1956-1957.

"The Compend: Addendum for the Year 1957", compiled by W. Hetherington, F.P.S.; 1958. Bristol: John Wright and Sons, Limited. 7¼" × 4¾", pp. 80. Price: 5s. (English).

This second addendum to "The Compend" contains monographs on approximately 220 new ethical products.

"Bulletins et Mémoires de l'École Nationale de Médecine et de Pharmacie de Dakar"; Volume V; 1957. Paris: Université de Daker. Expansion Scientifique Française, Editeur. 10¾" × 7", pp. 368, with many illustrations. Price not stated.

Contains papers (in French) on many aspects of medicine.

"Abstracts of Papers of the 54th Scientific Sessions of the Japanese Society of Internal Medicine"; 1958. Tokyo: The Japanese Society of Internal Medicine. 10¼" × 6¼", pp. 246, with many illustrations. Price not stated.

The sessions were held in Tokyo in April, 1957. The abstracts are all in English.

"Food for Better Performance", by R. C. Hutchinson, D.Sc.; 1958. Victoria: Melbourne University Press. 7¼" × 4", pp. 116. Price: 13s. 6d.

A discussion of food requirements in Australia.

"International Standards for Drinking-Water"; 1958. Geneva: World Health Organization. 9¼" × 6", pp. 152. Price: 20s.

Standards proposed by a WHO study group working on the basis of reports from various regional groups.

The Medical Journal of Australia

SATURDAY, OCTOBER 11, 1958.

EMPLOYMENT PROBLEMS OF PHYSICALLY HANDICAPPED PERSONS.

IT is generally acknowledged that if potentially employable disabled people are to gain employment, their needs must receive special attention. At times when the number of fit unemployed increases, this is especially so, and the relevance of problems inherent in survival to greater age, and in reduction in child mortality from previously lethal congenital and acquired defects, need scarcely be stressed. It must be obvious that if we are to view the difficulties faced by physically handicapped persons seeking employment against their true and wide background, we must examine the whole gamut of the activities of a community—maternal welfare, housing, care of the pre-school child, education (primary, general, technical, agricultural), apprenticeship training, other vocational training, industrial legislation, health insurance, national health service, and medical and hospital practice.

With this background in mind the Council of Social Service of New South Wales, an organization representing relevant welfare organizations both voluntary and statutory, recently undertook a pilot survey of certain difficulties encountered by the physically handicapped person in securing and maintaining employment. The findings of this survey have appeared in a booklet, 500 copies of which were produced by Standard Telephones and Cables Pty. Ltd., New South Wales, and have been distributed by the Council to various assisting and interested agencies and members of the public. That such a survey should have been attempted is to the credit of the Council. Necessarily the survey had to be limited in its nature and in its scope, and the Council has expressed its earnest hope that its effort will serve as a stimulus and a guide for others acting on behalf of physically handicapped people.

An epilogue to the account of the survey contains eleven recommendations, but it seems fair to say that they are not necessarily logical deductions made from the statistical data of the survey. They are more in the nature of generalized aspirations for improvement in various directions. However, the following specific recommendations are included: (i) That the Director-General of Education should be invited to confer with representatives of the Council of Social Service on relevant matters. (ii) That a committee should be established to consider: (*a*) the training of adult and handicapped persons, (*b*) amendment of the *Workers' Compensation Act* to encourage the insured handicapped person to seek employment, (*c*) the removal of unnecessary medical standards for admission to superannuation schemes. (iii) That assistance be sought whereby persons with certain disabilities could obtain motor vehicles for transport to work. (iv) That the shortage of professional social workers should be overcome by the provision of scholarships.

The report of the survey, after indicating the methods used, discusses certain relevant data, including physical limitations, family relationships, education, vocational training and "job status" before and after the onset of disability. Separate chapters are devoted to congenital disability, tuberculosis, epilepsy, blindness, deafness and dumbness, and mental deficiency. A well-documented section deals with information gleaned from reports obtained from certain employers. Special sections are concerned with the Commonwealth Employment Service and the Commonwealth Rehabilitation Service (contributed by the departments concerned), problems related to cerebral palsy (contributed by Dr. Claudia Burton-Bradley) and sheltered employment (presumably written by the authors of the survey). Appendices indicate the nature of the various *questionnaires* and take in certain relevant statistical and other data concerning employment.

By intention, the survey omitted those whose sole disability was psychiatric. The definition of a disabled person used refers specifically to a disability which has proved a substantial handicap in obtaining or keeping employment which, otherwise, would be suited to the age and qualifications of the person concerned. The disabilities are classified in a formal manner into various groups, including a miscellaneous group. This last-mentioned group is half as large as "locomotor", as large as "tuberculosis", and twice as large as "cardio-vascular"; it includes peptic ulcer, head injury, dermatitis, blackouts, diabetes and disseminated sclerosis. Some samples are so small as to render significant deductions out of the question. This is especially so in regard to epilepsy, in the section on which the lack of collateral medical comment, as in other parts of the survey, can only be regarded as somewhat conspicuous by its absence. Moreover, little evidence appears that attention has been paid to the need for adequate medical supervision of the placement of the handicapped. In the preface of the report it is noted that "members of the medical profession have advised on medical qualifications and work tolerance schedules"; but it is probably fair to say that had it been possible for enlightened medical support to have accompanied the survey more closely, the survey would have been more valuable. This, however, must not be taken as being in any way derogatory to the efforts of the authors of the survey.

One finding in particular should not be overlooked; that is that those persons suffering from "tuberculosis and unstable chronic conditions" do take more sick leave than those suffering from stable conditions, "amputations, deafness, etc.". To the former may be added nervous disorder. In this regard it is important to weigh such observations against some inadvertently misleading references from overseas to the excellent record of non-absenteeism of certain disabled workers. It is certain that highly selected groups of disabled people have better attendance records than their otherwise fit fellows. Obviously self-selected groups have more reason to continue working well, and to remain happy at work, than their more fortunate fellows. Thus the whole question is raised of the very difficult problem of motivation, an aspect of personal drive which cannot readily be accurately assessed, especially by the inexperienced. Many episodes of sickness result neither

in death nor in much time off work. Other illnesses and injuries may have the effect of making it impossible for the patient, if a scholar to continue his normal schooling, if a housewife to continue unaided to housekeep, or if a worker to return to his former employment. Because of the obvious importance of the intactness of a person's home and of the difficulty of finding light work not requiring special training or special skill, it is not surprising that this survey showed that the greatest difficulties in finding work were experienced by those disabled persons who suffered also from defective or poor intellect, lack of schooling, lack of trade training (using the term in its widest sense) and lack of the help which man in need must receive from spouse, blood relation or close friend if he is to weather various economic and physical storms.

As a recent editorial article[1] had to say of surveys of sickness particularly, we should ask ourselves what this type of investigation hopes to achieve. There is little doubt that the serious limitations of small surveys should be realized clearly by those who would interpret them. In the editorial article referred to, it was noted that it was a special feature of the British school of social research that attention had been focused largely on specific diseases—bronchitis, congenital abnormalities, coronary disease, peptic ulcer, tuberculosis—rather than on the wide approach to morbidity which was the subject of earlier inquiries. With surveys of employment problems of the handicapped, a somewhat different question presents itself, for it is, in certain regards, undesirable to focus attention on specific diseases. An interesting parallel is found in the opinion of the select committee of the British Medical Association in Britain on "The Rehabilitation and Resettlement of Disabled Persons" (1954), which recommended that the problems involved should not be tackled by the scheduling of various diseases—poliomyelitis, rheumatism and arthritis, etc. There are many valid reasons for this—it would create an unbalanced approach; many people bearing a disability label nevertheless consider themselves able-bodied and indeed may be unemployed at times for reasons quite unrelated to their "labelled" disability; some of the diseases are of unknown ætiology, and advances in medicine thus come to render the construction of special institutions superfluous or wasteful. Again, as noted elsewhere, patients may have multiple disabilities, the effects of any one or more of which may vary from time to time. Very importantly also, the practitioners in special centres and their patients tend to cut themselves off, or necessarily fall away, from the main stream of medical education, treatment and research.

There is a tenet which, although it may seem obvious, needs repeating—the disabled person must be trained so that he has a skill to sell. Thus the patient should be trained to the limits of his physical, mental and social potentialities (and this, of course, involves medical guidance). For those who cannot be trained because of some inherent mental, intellectual or other defect, the best possible selective placement must be achieved. Unfortunately, there will remain some who, despite their own best endeavours and those of the people whose role it is to help them, remain unemployed. These naturally include those of our fellow men and women whose mental limitations, maladjustment, emotional imbalance, defect of personality, physical impairment etc. are greatest. Included also are a high proportion of women over 40 and men over 50 years of age, especially those who have once been married or who are single, and who live alone or know few if any family ties. Some of these must remain in this unhappy state of unemployment for life; some by a surprising turn of events come to achieve a "niche of usefulness and self-respect".

As the specific and general recommendations indicate, the wider aspects of the impact of disability on our working adolescents and adults open up the important matters of education and of training of the type available in the Reconstruction Training Scheme of post-war years, as well as other numerous matters referred to above; in addition, the social implications of mental defect, low intelligence, chronic neurosis, loneliness, divorce, etc., which are often key factors in unemployment of the otherwise potentially employable disabled persons, must be noted. The field is so wide that there is enormous scope for more to be done, for more money to be spent, for more people to be trained, and for a certain diminution of agency-consciousness which is perhaps natural enough as a temporary symptom. There is a feeling in certain medical quarters that when adequately staffed rehabilitation departments come into being, they, fully supported by the major hospitals of which they are an integral part, will be uniquely placed to help, by both advice and action, in many aspects, if not indeed in the main aspects, of this field of social medicine. In the meantime it is only natural that mainly non-medical voluntary and governmental agencies should be doing what they can. It is to their credit that they have done so much for so long, and it is to be hoped that the support they need for their particular ultimate tasks will not be too long in coming. It will require a realization on the part of the legislature and hospital boards that for rehabilitation to pay dividends, the investment must be made, albeit wisely made. This report of a pilot survey of the Council of Social Service of New South Wales cannot but focus the attention of many interested people and groups on this problem. It is to be hoped not only that its voice will find suitable company, but also that the placement of the disabled will come to rest securely on the firm basis of enlightened medical supervision as an integral part of modern medical and hospital practice.

[1] *Brit. M. J.*, 1958, 1: 329 (February 8).

Current Comment.

TUBERCULOSIS AND SALMONELLOSIS AS ZOONOSES.

Cattle are becoming much less important as a source of transmission of tuberculosis to man in many countries. At the same time, public health authorities are paying more attention to other animal sources of tuberculous infection, notably dogs, cats, parrots, goats, pigs and monkeys. During the last few years, rapid progress in the control of bovine tuberculosis has been reported from Portugal, the United Kingdom, the German Federal Republic and Switzerland. In the Scandinavian countries, the Netherlands and the United States of America, this disease is now practically non-existent, mainly as the result of systematic application of the tuberculin test in cattle and slaughter of all animals reacting to this test. This progress was noted with satisfaction by the Joint Expert

Committee on Zoonoses of the World Health Organization and the Food and Agriculture Organization during a recent meeting in Stockholm. In countries where bovine tuberculosis is still an important problem, approximately 10% of human infections are derived from cattle.

The discussions at the meeting revealed that dogs can become infected with either human or bovine tuberculosis. Cats are resistant to the human type but susceptible to the bovine type. Parrots can contract human tuberculosis. Monkeys are highly susceptible to both types. However, animals can also become infected from humans, and many cases of reinfection of tuberculosis-free cattle with human or bovine type strains have been traced to this source.

Among other zoonoses (about 80 have so far been listed) reviewed by the WHO and FAO experts were the salmonelloses. Human salmonellosis is frequently fatal to the very young and the very old and is responsible for much minor disability and discomfort in persons of all ages. It is common in many countries, and appears to be on the increase. In England and Wales, for example, about 3000 cases are reported annually. In the German Federal Republic numerous outbreaks associated with sausage, boiled ham, pork, eggs and cheese have been reported in recent years. In Sweden some thousands of cases have occurred from the consumption of both home-killed and imported meat. In the Netherlands, many outbreaks have been traced to meat products. A recent survey shows that of 200 outbreaks of salmonellosis associated with food, five came from fresh meat, 87 from processed or made-up meat, 41 from eggs (mainly ducks' eggs) and egg products, 23 from cream confectionery, 10 from milk and 34 from other foods. Recently it has also become known that animal feeding stuffs and fertilizers may be contaminated with salmonellæ. In some European countries it has been found that some types of salmonellæ previously unknown locally have been imported with feeding stuffs and fertilizers, causing outbreaks of the disease both among animals and humans. The discussion at the WHO/FAO expert meeting on preventing salmonellosis stressed the importance of reporting all human cases, education of food handlers in a high standard of hygiene, proper refrigeration of food products, effective pasteurization of milk, and sterilization of animal feeding stuffs.

ASIAN INFLUENZA.

According to a statement recently issued by the World Health Organization, the A/Asia/57 virus, which last year took the world by surprise, is likely to be the predominant type in influenza outbreaks during the next few years. People who were infected during the pandemic in 1957 are likely to have at least a basic immunity to the virus, and it is therefore possible that they will escape infection if any local epidemics do occur. The most striking fact with regard to the 1957 influenza pandemic, which was reviewed recently at a meeting in Stockholm by the Expert Committee on Respiratory Virus Diseases of the World Health Organization, is that the virus responsible is quite distinct from any of the viruses which have caused epidemics during the recorded history of influenza viruses, i.e. since 1933. Since most population groups had never been in contact with the "new" virus, and consequently had not acquired immunity to it, the advance of the pandemic met with little resistance. It affected almost half the world's population. However, compared with previous major influenza outbreaks (the 1918-1919 pandemic, for example, is believed to have killed at least 15 million people) the 1957 pandemic remained mild. New outbreaks of "Asian influenza" may prove even milder, because the natural resistance built up last year will make it more difficult for the virus to get about. Also, large quantities of vaccine, proved to offer 60% to 70% effective protection, are now available in several countries. According to the WHO experts, vaccination, from a clinical point of view, is especially important for expectant mothers and for people suffering from cardio-vascular or lung disease, or metabolic disorders. To offer maximum protection, vaccination should be given at least two weeks before the period when influenza is expected to become epidemic.

During their meeting in Stockholm, the WHO experts reviewed important new advances in influenza vaccine research. It is stated that experience in the U.S.S.R. with attenuated live virus vaccines appears promising. The principles guiding the development of live virus vaccines are to produce a preparation that is maximally effective, is economic and can be administered easily with the least discomfort to the recipient. In contrast to the formalin-inactivated influenza virus, now in general use in most countries, the live virus vaccine is not administered by inoculation, but sprayed into the nose and throat. Because of its high virulence, it is not recommended for children less than seven years of age. Another solution, promising but as yet unproven, to the problem of producing sufficient quantities of a certain vaccine fast enough when a new strain of virus is about is to make the quantity of ordinary vaccine go further by mixing it with an "adjuvant". This will enhance the effect of the vaccine so that less is needed per dose. At the same time, whichever vaccine is used, there can be no question of stopping an influenza epidemic by vaccination. What is aimed at is the limitation of its effects by preventing high death rates and excessive absenteeism, such as would disorganize public services and bring society to a standstill.

The WHO experts also reviewed the possibility of an animal reservoir of human influenza. It has been shown that a virus related to the influenza virus of swine was prevalent in man about the time of the 1918-1919 pandemic, and it is possible that the same or a closely related virus may have been the cause of that pandemic. The possible relationship of the Asian virus to a virus present in man about the time of the 1889 pandemic and the postulated reemergence in 1957 of the 1889 virus from some unknown situation, *plus* the fact that the swine virus no longer affects man but persists in pigs, have raised the possibility that certain animals may play a role in the ecology of human influenza. This is at present speculation, but several important studies, initiated by WHO, are in progress; if it proves to be correct, it will be a major advance.

Among other viruses causing respiratory infections discussed at the meeting in Stockholm were the adenoviruses. Several types of these have been identified recently. The attack rates of febrile cases of the disease may reach 25% during the winter among people crowded together—for example, military recruits—but the rates in summer are usually low. Summer epidemics caused by types of adenoviruses have been observed especially among children. These epidemics may have been related to contamination of swimming pools and lakes. Some of the adenoviruses have been incriminated as the cause of epidemic respiratory diseases, and some can infect the eye, causing a form of conjunctivitis. With regard to the common cold, one of the major pests of mankind, the WHO experts reviewed evidence that it is not caused by a single virus but may be due to a number of different agents. We are still a long way from a solution to this baffling problem. Application of new techniques, however, gives more hope for the future.

In reviewing the influenza programme carried out by WHO, the international experts agreed that the world-wide network of WHO influenza centres had already contributed much to the knowledge of the endemiology and control of influenza. In just less than three weeks after WHO had received the first news that a significant epidemic was occurring, the Organization was able to inform health authorities and vaccine-producing laboratories that the responsible virus was unrelated to all previously isolated strains and that existing vaccines were unlikely to give protection. This warning was given in time for several countries to "race" the impending epidemic. The first notification of the "new" virus was sent to WHO from Singapore on May 4, 1957. However, as was afterwards discovered, the epidemic had already been spreading for eight weeks in mainland China, which is not at present participating in WHO's work. If this had been known at the time, the world would have had two more months in which to prepare.

Abstracts from Medical Literature.

DERMATOLOGY.

Penicillin in Milk.

H. R. VICKERS, L. BAGRATUNE AND S. ALEXANDER (*Lancet*, February 15, 1958) discuss dermatitis caused by penicillin in milk. The incidence of sensitivity to penicillin is probably about 5% for the general population and 12% to 15% for those engaged in its manufacture or who have multiple allergies. Since the introduction of machine milking, the incidence of mastitis in cows has increased, and the common practice of herdsmen is to inject 100,000 units of procaine penicillin into the teat of the infected quarter. As a result of this treatment milk may contain penicillin. If patients previously sensitized to penicillin by local application drink milk containing penicillin, dermatitis may develop and persist indefinitely if its true nature is not recognized. The authors report two cases of patients in whom penicillin in milk seems to have been the cause of dermatitis. Naturally, those living on dairy farms will be more liable to a high penicillin intake than the general population, which benefits from more extended bulking with consequent dilution of the penicillin content.

Antibiotics in Dermatology.

G. B. MITCHELL-HEGGS (*Practitioner*, May, 1958) discusses the use of antibiotics in dermatology. The treatment of minor skin infections with the powerful wide-spectrum antibiotics is not only unnecessary but is also a disservice to medical therapeutics generally. The development of resistance to the antibiotics, especially by the staphylococcus, is now of major importance in most branches of medicine and surgery and especially so in hospital practice. Knowing that immunity can occur, we have to tread very cautiously when considering the use of antibiotics in any skin disorders. The indiscriminate use of antibiotics in dermatology may lead to a further increase in the number of resistant strains of various organisms. Routine bacteriological confirmation of the presence of the organism and its specific antibiotic sensitivity should be made for all patients receiving hospital treatment, and when practicable in general practice. The decision should then be made between systemic and local administration. A previous history of sensitization reactions to penicillin, however small, contraindicates its use. It may be necessary to resort to the group of wide-spectrum antibiotics. If topical application is required, penicillin, chloramphenicol and streptomycin should be used with the greatest care because of their marked propensity to produce epidermal sensitivity. It is preferable to use as first choice a substance that is not used systemically, such as neomycin, bacitracin or "Soframycin". These substances do not easily cause sensitization and are effective in their action. Prolonged systemic use of antibiotics will bring about a rapid increase in resistant bacteria and monilia and more cutaneous moniliasis is now seen. The author discusses the indications for the use of antibiotics in dermatology in the following conditions: persistent skin infection, impetigo, ecthyma and pemphigus neonatorum, erysipelas and cellulitis, folliculitis barbæ and sycosis barbæ, hydradenitis suppurativa, acne vulgaris, stasis ulcer, paronychia, pustular bacterid pemphigus, acrodermatitis of Herxheimer and lichen planus. He states that hypersensitivity reactions occur most commonly with the administration of penicillin and occur in 1% to 5% of patients. In the early days of penicillin therapy, indiscriminate use of topical penicillin led to the frequent development of epidermal sensitivity, presenting as acute eczema. In systemic therapy the immediate reaction takes the form of acute anaphylaxis and may prove fatal. The delayed reaction which may occur from 24 hours to four weeks after administration of the drug is variable, but usually takes the form of serum sickness, which includes pruritus and urticaria.

Cutaneous Porphyria with Porphobilinogenuria.

S. M. WOODS, H. R. PETERS AND S. A. M. JOHNSON (*Arch. Dermat.*, May, 1958) present a case of hepatic porphyria of the cutanea tarda variety in which there was evidence of latent and manifest porphyria in the maternal blood line. Chelation therapy with heavy-metal chelates such as dimercaprol (BAL) and "Calcium Disodium Versenate" in the treatment of acute intermittent hepatic porphyria has been highly favourable. The patient's apparent favourable response to "Calcium Disodium Versenate" is encouraging and suggests the need for further evaluation of chelation therapy in the treatment of porphyria. A number of other patients were moribund while under steroid and other forms of therapy until chelation was begun.

Arsenic in the Skin.

A. SCOTT (*Brit. J. Dermat.*, June, 1958) discusses the retention of arsenic in the late cutaneous complications of its administration. The properties of irradiated arsenic may be used to assay that substance in small amounts of tissue. The normal levels of arsenic in human skin are consistently below 1·0 milliequivalent per gramme. Patients who have been exposed to arsenic, either through its ingestion or by external contact, and who have later developed keratoses and epitheliomata, tend to have a higher than normal content of arsenic, not only in the actual lesion but also in their normal skin. There is an individual variation in the ability of persons to eliminate arsenic.

Tinea Nigra Palmaris.

J. G. SMITH, JUNIOR, AND F. J. ROTH, JUNIOR (*J.A.M.A.*, May 19, 1958) discuss tinea nigra palmaris, a disorder easily confused with junction nævus of the palm. This is an uncommon skin disease caused by the fungus *Cladosporium wernecki*. Nearly all reported cases have involved the palms. The asymptomatic macular lesions, neither elevated nor scaly, are brown or black, appearing like an indian ink or silver nitrate stain. The disease must be differentiated from nævi, contact dermatitis, the pigmentation of Addison's disease, and drug eruptions. The pigmented lesions of photodermatitis due to bergamot or lime oil can be differentiated easily, since they never occur on the palms. The disease is asymptomatic, and responds readily to local therapy with keratolytic agents such as salicylic and benzoic acids. Attempts at experimental reproduction by inoculation of infected scales and fungus itself into the epidermis of human volunteers were unsuccessful.

Psoriasis.

W. B. SHELLEY AND D. M. PILLSBURY (*J.A.M.A.*, June 21, 1958) state that triamcinolone, a new fluoroprednisone compound, has been shown to have a significant temporary suppressive effect on psoriasis. Thirty-six of a series of 60 consecutive patients with psoriasis proved to respond rapidly and dramatically to from 12 to 16 milligrammes of triamcinolone daily. This group presented the distinctive finding of local involution of psoriasis at the site of injection of triamcinolone intradermally. Relapses invariably occurred when the triamcinolone therapy was withheld. Topical triamcinolone therapy was without effect in the treatment of psoriatic lesions. On the basis of this experience the authors reserve triamcinolone for acute extending psoriasis not controllable by other means, or for very extensive and severe chronic psoriasis. Side effects of triamcinolone therapy in the dosage employed by the authors were similar to those seen with other corticosteroids. No evidence of hypertension, œdema or hyperglycæmia was found. In five patients changes developed resembling those of Cushing's syndrome, and hirsutism was found in four patients. The dosage employed with most success was four milligrammes taken orally four times a day.

Tinea Pedis.

G. A. G. PETERKERR (*Practitioner*, May, 1958) discusses the diagnosis and treatment of tinea pedis. He states that without cultural proof it is not possible to determine by clinical or microscopic study the type of fungus present. Tinea rubrum is notoriously resistant to treatment. There are four main clinical groups: (i) macerated lesions, (ii) vesicopustular lesions, (iii) squamous lesions, (iv) keratotic lesions. The toe-nails may be involved. Even if fungus is demonstrated it does not follow that all or even the greatest part of the patient's dermatosis is due to the fungus; he may have a contact dermatitis as well. Macerated lesions between the toes are not all due to fungi. Often hyperidrosis of the feet is mistaken for tinea. Intertrigo or flexural infective eczema may occur between the toes just as it can appear in the natal cleft, or in the submammary region. Eczematous reactions are often mistaken for dermatophytosis, especially contact dermatitis, which is often caused by footwear (e.g., rubber, dyes, glues). Pompholyx or dyshidrosis may be difficult to distinguish from tinea. Post-traumatic infective eczema is sometimes located on the feet; an example of this type is dermatitis repens due to a staphylococcal

infection with undermined edges. Recalcitrant pustulo-squamous dermatoses also simulate tinea, e.g., pustular psoriasis, pustular bacterid and acrodermatitis perstans pustulosa. Lichen planus may affect the feet, also lichen simplex chronicus, keratodermia climactericum and drug eruptions. Accurate diagnosis of tinea pedis must be based on sound evidence, as there are so many pitfalls. Therapy is not merely an attempt to destroy, by means of more and more potent fungicides, the tinea invading the superficial layers of the skin. Often potent chemicals do far more harm than good. The discovery of nystatin makes a real advance in therapy, as this has a remarkable effect on *Candida albicans* and it can be given orally as well as locally. Tablets containing 500,000 units given four times a day often give remarkable results. The author proceeds to discuss in detail the treatment of the different clinical types of tinea infections. He states that for macerated interdigital tinea, powder, paints or wet dressings are preferable to ointments. When vesiculation or pustulation is apparent, it should be treated as an acute infective eczema with wet dressings of strong (5%) solution of lead subacetate, or undiluted aluminium acetate solution. For infected tinea he recommends "Quinolar" ointment or vioform ointment, perhaps with the addition of 1% hydrocortisone to control pruritus and inflammation and to prevent reactions due to the other drugs. The use of antibiotics such as penicillin, chlortetracycline and oxytetracycline whether applied locally or used internally is strongly contraindicated. Sulphonamides taken orally may be used instead. Whitfield's ointment is recommended for squamous ringworm. For tinea rubrum "Asterol" ointment or dithranol, 0·5% in Lassar's paste or 2% in soft paraffin, is among the most effective.

UROLOGY.

Urethritis in Female Patients.

C. EBERHART (*J. Urol.*, February, 1958) states that in diseases of obscure ætiology treatment is usually varied and often unsatisfactory; such is the status of urethritis in females. Formerly, this morbid condition was assumed by some to be due to interstitial infection of the whole of the distal part of the canal, but amputation of the distal centimetre of the canal failed to give good results. Destruction of the entire urethral mucosa proved even more disappointing. However, recent studies have shown that the infection originates in the para-urethral glands; unroofing of their ducts has brought encouraging results. The para-urethral glands (Skene's glands) and their ducts are homologues of the prostate gland, and their orifices open in a postero-lateral position, just within the external meatus of the urethra. Here they are submucosal; more proximally they become deeper and their proximal ends are in contact with the internal sphincter muscle. Normally, the urethral mucosa possesses natural defence against the bacterial flora of the vulva, but when the gland wall is invaded by germs a low grade of inflammation of the entire duct occurs. This results in scarring and partial occlusion of the gland. The presence of the proximal portion of the inflamed gland within the grasp of the internal sphincter causes symptoms of urethritis to appear. When bacteria from the inflamed gland are discharged on the bacterial mucosa, they infect the bladder, causing secondary cystitis. It has been found that the most effective treatment is to avulse or tear away the roof of the entire duct and gland, including the overlying urethral mucosa. A panendoscope is passed, and then a grooved director with a fine ball-pointed probe end is passed alongside the instrument into the field of vision. In the author's series the orifices of the urethral glands have always appeared normal. Under this vision the probe is easily inserted into each orifice just within the external meatus. It is passed up along the duct and its tip is finally elevated and made to puncture the mucosa just distal to the internal meatus to prevent damage to the internal sphincter. The slightly upcurved probe-tip emerges in the beak of the sheath, and both are simultaneously withdrawn. This tears a furrow in the urethral mucosa. This is done on both sides. A large Foley catheter is left in for four days to prevent closing over of the edges of the furrow.

Vesical Diverticulum.

ASHTON MILLER (*Brit. J. Urol.*, March, 1958) has made an intensive study of the whole problem of vesical diverticulum, from the point of view of both pathogenesis and of treatment. The study included 105 cases of diverticulum of the bladder seen at two British hospitals during the years 1950 to 1954, inclusive. Specimens obtained at operation or autopsy were examined in detail. The youngest patient was an infant of 15 months, the oldest a man of 93 years. There were four women among the 105 patients. The presence of five children and of 12 adult patients under 45 years of age indicates that there is an ætiological factor other than acquired urethral obstruction due to enlarged prostate stricture. In every case in the present series it was possible to demonstrate hypertrophy of the bladder wall. The hypertrophy chiefly affects the inner of the three coats of muscle tissue. It is considered that urethral or bladder neck obstruction is always congenital. The mucosa bulges under the influence of increased intravesical pressure through separate bundles of the net-like inner coat of muscle. It is probable that the pouch always remains within the tissues of the bladder wall, with some of the outer two coats of muscle always covering it. While the saccule is shallow, contraction of the bladder wall will empty it, but when it is deeper contraction of the inner coat of muscle narrows the neck of the sac, while increased intravesical pressure forces urine into the diverticulum and blows it up more and more. Congenital bladder-neck hypertrophy is thought to affect the internal sphincter muscle. It is suggested that a child can be born with a bladder neck obstruction and already have a hypertrophied bladder wall. This can occur in both sexes. If the obstruction is severe, symptoms occur early, but they are delayed if the obstruction is adequately compensated by hypertrophy of the bladder wall. Senile hypertrophy of the prostate is considered to be an acquired obstructive factor additional to whatever thickening of the bladder neck already exists. A diverticulum develops if a small saccule of bulging mucosa can find a suitably large gap in the network of muscle bundles of the inner muscle coat. Such a condition does not often exist, therefore relatively few cases of bladder-neck obstruction develop a diverticulum. It is necessary in all cases to remove the bladder neck obstruction, and this is done by endoscopic resection. If, as is unusual, the prostate is grossly hypertrophied, open removal is better. This is sufficient in cases of small, well-emptying diverticula, but when the diverticulum holds much residual urine after urination it should be removed as well. This is determined by pre- and post-micturitional cystography. The author prefers to do diverticulectomy first, then, a week or two later, to perform an endoscopic resection. The author advises a simplified type of operation, in which an incision is made through the bladder wall, just large enough to admit the left index finger, which is passed into the diverticulum. The bladder wall is mobilized until the neck of the diverticulum is seen. The neck of the diverticulum is carefully divided so that the sac is isolated from the bladder. The mucosa lining the isolated sac is peeled off, or the sac is drained to the exterior. The bladder wall is closed completely, and the bladder drained by an indwelling catheter.

Primary Tumours of the Ureter.

L. G. WOOD AND G. E. HOWE (*J. Urol.*, March, 1958) present nine cases of primary tumour of the ureter. Two were definitely benign and a further case was classified as benign, though potentially malignant, being a papilloma; in this case a complete nephro-ureterectomy was performed. The remaining six patients had transitional cell carcinomata and were treated as follows: one by complete nephro-ureterectomy; one by fulguration of the tumour which was in the ureteric orifice (this patient died of myocardial infarction eight months later and no sign of neoplasm could be found); the remaining four were treated by subtotal nephro-ureterectomy, and all were alive six months to eight years later. While the authors believe that the ideal treatment of malignant tumour of the ureter is complete nephro-ureterectomy (including the whole intramural ureter), excellent results have been obtained in selected cases by the subtotal operation (dividing the ureter just outside the bladder). Clinically, whenever pain is due to a ureteric tumour, hydronephrosis can be demonstrated urographically. The authors quote the important dictum of Abeshouse: "One should remember that infiltrating ureteral neoplasms are frequently diagnosed as strictures of the ureters, and stricture of the ureter with accompanying hydronephrosis is rare in patients of the carcinoma age group. For all intents and purposes, stricture of the lower third of the ureter in this age group should be regarded as malignant until proven otherwise."

Special Article.

SAVING FOR RETIREMENT.[1]

IN these days, most people who are employed, particularly those employed in a semi-professional or administrative capacity, become members of a superannuation plan which provides reasonably for their after-retirement needs. With some such plans, the whole cost is paid by the employer; with practically all of them not less than half of the cost is so paid.

For the man in professional practice, however, the whole task of providing, during his professional career, sufficient to meet the needs of himself and his dependants after he retires must be carried by himself. There are usually three alternative methods by which he may perform it:

1. He may accumulate savings privately by making suitable investments.

2. If a suitable fund is available which he is eligible to join, he may contribute to a trust fund set up under Section 23 (ja) of the *Income Tax Act*.

3. He may effect a suitable life assurance policy or policies.

If he chooses method 1, he can hardly avoid exercising supervision over his investments, including such matters as determining the amounts to be invested, the dates at which those amounts are made available, the types of investment to be selected and even the individual investments within those types. He must also keep a record of his investments and of the income from them (or arrange for this to be done for a fee), must arrange for the re-investment of money when an original investment matures, and should have regard to the desirability or otherwise of changing investments from time to time. It is hardly practicable to carry out this investment programme efficiently in the odd moments (if any) which a busy medical man can spare from his own practice.

Further, it is only the most strong-minded of individuals who can sustain a systematic investment programme by putting aside regular amounts at fixed intervals for the purpose, if the programme remains completely private and voluntary.

Under this method, also, interest received from the investments is fully taxable except for the minor concession given in respect of Commonwealth Government Securities. This means that, as compared with any method which removes the investment income from the doctor's own income tax return, the interest income must be regarded as being subject to tax at the rate applicable to the top segment of his income. If, for example, his taxable income, apart from these investments, would be £5000 *per annum* and he receives in a particular year £500 from interest income, this would be subject to tax (at present rates) of 11s. in the pound, leaving the net investment income £225 only.

Under method 2 or method 3, investment problems are taken care of by the trustees of the fund or by the life assurance office respectively, and the interest income is not taxable in the hands of the doctor. Further, under either of these methods, up to £300 *per annum* of the contributions he pays can be deducted from his taxable income, thus saving tax on this amount at the rate applicable to the top £300 of his income. Either of these methods, therefore, offers such a considerable advantage over private investment that the latter should hardly ever be considered as a major method of saving.

Let us look then at the differences between method 2 and method 3. With the former, the fund must be subject to rules which are approved by the Taxation Commissioner. Among other things, these rules will certainly provide that no individual member's interest in the fund can be withdrawn earlier than his reaching a suitable retiring age (usually 65 years) except in the case of his death or in the case of his becoming so permanently disabled that he is unable to continue practice. These necessary conditions would also prevent the doctor's interest in the fund being used as security if he wanted to borrow money in order to purchase a home or practice. He could decide to cease paying contributions, or presumably decrease the rate of contribution he is paying, but the amount available from whatever contribution he does pay would still come to him only in the events mentioned.

Such funds have the advantage of freedom from taxation by virtue of Section 23 (ja) of the *Income Tax Act*. The results they can achieve for their members will depend on a number of other factors, however, such as the type of investment selected and the degree of skill and attention which the investments receive. The degree of security enjoyed by the members will also vary as between different funds of this type, which will probably vary greatly as to size and as to efficiency of management. Apart from the requirement that their rules be approved, there is no provision for supervision of the operations of funds established under this section.

If method 1 or 2 is used, the doctor should make sure that a suitable part of his contribution is used to provide life assurance cover, or should provide for such cover himself by some separate action; otherwise there will certainly be insufficient protection for his dependants if he dies fairly early in the period of accumulation.

If such cover is effected by means of an endowment assurance policy maturing at the age he expects to retire, it will probably require a substantial part of the available contribution to provide sufficient cover; in respect of this part of his contribution, the doctor is then in effect using method 3. An alternative is to effect temporary assurance cover only, ceasing at or a few years before retiring age. This would use a much smaller part of the contribution, but the assurance so effected would never have any cash value and would lapse immediately if payment of premiums were ever discontinued. It would probably not carry any right to participate in the surplus of the assurance company.

Under method 3 the doctor can choose, out of a fairly wide variety, the type of policy contract best suited to his needs, and he can retain the ownership of his policy. That being so, he can use it as security for a loan; or if his circumstances alter, he can change it to a more suitable type. If he finds that he cannot continue premium payments, he can make the policy paid-up for a reduced amount and thus still keep some degree of assurance cover; or if it has been in force for some years, he can surrender it for a cash sum.

A life assurance policyholder has the advantage of participating in an established portfolio of investments, within which it is probable that contingency reserves have been provided. The degree of security involved is therefore very high indeed, and is improved by the control and publicity provided by the *Commonwealth Life Insurance Act* and the appointment of an actuary as Insurance Commissioner under that Act. Major offices are of such size as to employ specialist investment departments, which keep continual watch on the investments of the office and make changes in investment practice as current conditions indicate. While life assurance offices are not completely free from tax, they are taxed on a special basis which relieves a substantial part of their investment income from tax liability.

It has been claimed that one advantage of a separate fund established under Section 23 (ja) is that it has the opportunity of investing a large proportion of its funds in ordinary shares, and that if further inflation occurs, the values of these shares will tend to increase, thus offsetting the effect of inflation in reducing the real worth of retirement or death benefits. There are, however, dangers in pursuing this idea too far. Investigation has shown some correlation between share prices and the purchasing power of money, but this is by no means perfect; it will not follow that when a retirement benefit is payable at a time of high price level the share market will necessarily be buoyant at the same moment.

Large-scale investment of a fund's assets in ordinary shares, in a search for a higher (tax-free) interest return, with possible capital gain, designed as a complete "hedge" against inflation, is of advantage only if present conditions continue. Even if they do, this method is full of dangers—it depends completely on skill in investment, on economic and perhaps even political conditions, and on an absence of large withdrawals for many years; there is, moreover, no guarantee of security such as a life office can give, and special funds may be necessary to absorb the shock of any future major disturbances. If the retirement benefits of a member depend on the current values of the fund's assets, the results for those members who retire at a time of depressed share prices could be very unfavourable.

Life offices are not neglecting the field of investment in ordinary shares, but are proceeding cautiously. Their holdings in this class of investment are still modest (in comparison with their funds as a whole), but are growing rapidly; and, if the theory about future increases in share values proves correct, holders of policies participating in distributions of surplus will ultimately benefit.

[1] This article, prepared by the Life Officers' Association for Australasia, is published for the information of the medical profession. The views expressed are not necessarily those of this journal.

It is hoped that by setting out the pros and cons of the three possible methods of provision for retirement, doctors will be helped to choose the one they feel to be most appropriate to their circumstances. On balance it would seem that they should use life assurance as their main avenue for such provision and thereby obtain security, protection for their dependants and a high measure of tax-saving, while still retaining the right to deal with their own asset.

Hospitals.

CANCER OF THE WOMB, 1930-1957: TREATMENT RESULTS AT THE KING GEORGE V MEMORIAL HOSPITAL, ROYAL PRINCE ALFRED HOSPITAL, COMPILED DECEMBER 31, 1957.

CANCER is one of the diseases which as yet the medical scientists have been unable to conquer entirely and one which the public fears most. In the last century millions of pounds have been spent in laboratories and their allied workshops, the clinical hospitals, with only slow curative progress.

Many public cooperators in the fight against cancer mix up statistical information regarding surface or skin cancer and internal or deep-seated cancer. These two types of cancer should always be recorded separately. The staff of the King George V Hospital can give factual information about the treatment of only one section of internal cancer, namely, that of the womb, its appendages and the vulva.

Cancer of the Cervix Uteri.

The staff of the King George V Hospital have followed out one form of treatment since 1930, which, if not the right method of attack for complete success, at least gives basic figures and shows much progress in the saving of Australian lives.

The routine method of treatment for carcinoma of the cervix has been since 1930 the pre-operative application of 70 milligrammes of radium for 100 hours, followed (whenever the lesion was thought removable) five to six weeks later by a radical Wertheim's hysterectomy with, of course, a thorough lymphadenectomy of the draining lymph glands.

TABLE I.

Royal Prince Alfred Hospital, Sydney, N.S.W.—Carcinoma Cervicis Uteri, 1930 to 1952: Five-Year and Ten-Year Cure and Survival Rates.
(Compiled December, 1957.[1])

Observation.	Five Years.	Ten Years.
All patients examined with a view to treatment ..	1047	689
All patients treated	993	650
Alive without recurrence	378	174
Alive with recurrence	14	2
Died of carcinoma	607	478
Died of intercurrent disease (under five and ten years)	20	21
Lost or not followed up	28	14
Cure rate amongst all patients examined	36·1%	25·2%
Survival rate amongst all patients examined ..	37·4%	25·5%
Cure rate amongst all patients treated	38·1%	26·8%
Survival rate amongst all patients treated.. ..	39·5%	27·1%

[1] Up to December, 1957, 1436 patients were examined with a view to treatment: 777 patients were treated surgically (operability rate, 54·1%); 24 patients died after operation (operative mortality rate, 3·08%).

Those patients clinically deemed unfit for the Wertheim's operation after having had the routine pre-operative irradiation are submitted to further radio or cobalt therapy.

Since the last Annual Report at the end of 1956 there is some all-round improvement in the statistics.

TABLE IIA.

Royal Prince Alfred Hospital, Sydney, N.S.W.—Carcinoma Cervicis Uteri: Five-Year Survival Rates, 1930 to 1952.
(Compiled December, 1957.)

Technique.	Stage 0.		Stage I.		Stage II.		Stage III.		Stage IV.		Total.	
	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.
Application of radium and/or surgery	23	19	92	69	265	155	154	74	—	—	534	317 (59·4%)
Application of radium alone ..	—	—	11	7	78	19	243	40	100	6	432	72 (16·7%)
Application of radium *plus* incomplete surgery	—	—	2	1	6	0	15	2	4	0	27	3 (16·7%)
No treatment	—	—	—	—	—	—	4	0	50	0	54	0 —
Total	23	19	105	77	349	174	416	116	154	6	1047	392 (37·4%)

TABLE IIB.

Royal Prince Alfred Hospital, Sydney, N.S.W.—Carcinoma Cervicis Uteri: Ten-Year Survival Rates, 1930 to 1947.
(Compiled December, 1957.)

Technique.	Stage 0.		Stage I.		Stage II.		Stage III.		Stage IV.		Total.	
	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.	Number.	Alive.
Application of radium and/or surgery	9	8	40	23	144	64	116	48	—	—	309	143 (46·3%)
Application of radium alone ..	—	—	6	1	52	11	180	17	85	3	323	32 (9·9%)
Application of radium *plus* incomplete surgery	—	—	1	1	5	0	9	0	3	0	18	1 —
No treatment	—	—	—	—	—	—	2	0	37	0	39	0 —
Total	9	8	47	25	201	75	307	65	125	3	689	176 (25·5%)

The cure rate of all patients seen since 1930 is as follows: in 1956, 34·8% (five years) and 24·6% (ten years); in 1957, 36·1% (five years) and 25·2% (ten years). The survival rate of all patients treated since 1930 is as follows: in 1956, 37·8% (five years) and 26·3% (ten years); in 1957, 39·5% (five years) and 27·1% (ten years).

TABLE III.

Royal Prince Alfred Hospital, Sydney, N.S.W.—Carcinoma Cervicis Uteri, 1948 to 1952: Survival Rate during Most Recent Five-Year Period.

Observation.	Five Years.
All patients examined with a view to treatment..	361
All patients treated	347
Alive without recurrence	156
Alive with recurrence	4
Died of carcinoma	172
Died of intercurrent disease under five years ..	5
Lost or not followed up	24
Cure rate amongst all patients examined ..	43·2%
Survival rate amongst all patients examined ..	44·3%
Cure rate amongst all patients treated	45·0%
Survival rate amongst all patients treated ..	46·1%

The operability rate of all patients seen moved from 53·7% to 54·1%; the mortality rate after operation improved from 3·15% to 3·08%. The number lost or not followed up increased from 20 to 28 (five years) and from 12 to 14 (ten years). There is reason to believe that some of these are alive, but the great flood of migrants to Australia in recent years makes the follow-up more difficult, as newcomers move from State to State and from town to town. Furthermore, some are not proficient in the English language and cannot understand or answer the questions asked. However, all lost patients are recorded as dead.

The total number of patients submitted to radical surgery was 534, and the number found to have involved glands was 115 (21·5%).

This is the picture of the over-all statistical facts since 1930, but owing to improved surgical technique, better nursing and after-care, better anæsthesia, the use of antibiotics and a more ample blood service, the last five years' statistics (1948-1952) have shown a commendable advance over the over-all statistics since 1930. The survival rate amongst all patients treated rose from 39·5% to 46·1%.

It is certain that, with cytology (Papanicolaou smear) and colposcopy discovering earlier and earlier cases not even recognizable to the naked eye, better figures will be obtained in the future years. In just over two years to July 1, 1958, a total of 2522 Papanicolaou smears and 405 colposcopic examinations have been performed at King George V Memorial Hospital. Ten cases of carcinoma of the cervix, none of which gave any clinical evidence of malignancy, have been discovered by these means. We have been surprised at the present neglect of the method of colposcopy in the U.S.A. and Great Britain, where almost complete reliance is placed on cytology for early detection. We agree with many Continental clinics that the best results are to be obtained by their complementary use.

Carcinoma of Corpus Uteri.

The figures for carcinoma of the body of the uterus treated up to 1952 are shown in Table IV. It will be seen that the five-year cure rate of all patients seen since 1930 is 57·5% and the ten-year cure rate is 43·0%. The survival rates for all patients treated are 62·2% and 44·5% respectively.

It has been the unanimous opinion of the medical staff that treatment of this disease should almost always be surgical. Treatment by radiotherapy alone has given poor results in our hands. The operability rate of 435 patients examined with a view to treatment from 1930 to 1957 is 76·6% and the operative mortality 2·1%.

TABLE IV.

Royal Prince Alfred Hospital, Sydney, N.S.W.—Carcinoma Corporis Uteri, 1930 to 1952: Five-Year and Ten-Year Cure and Survival Rates. (Compiled December, 1957.[1])

Observation.	Five Years.	Ten Years.
All patients examined with a view to treatment	261	142
All patients treated	254	137
Alive without recurrence	150	61
Alive with recurrence	8	0
Died of carcinoma	75	56
Died of intercurrent disease (under five and ten years)	17	19
Lost or not followed up	11	6
Cure rate amongst all patients seen	57·5%	43·0%
Survival rate amongst all patients seen	60·5%	43·0%
Cure rate amongst all patients treated	59·1%	44·5%
Survival rate amongst all patients treated.. ..	62·2%	44·5%

[1] Up to December, 1957, 435 patients had been examined with a view to treatment: 335 patients were treated surgically (operability rate, 76·6%); seven patients died after operation (operative mortality rate, 2·1%).

As with carcinoma of the cervix, the most recent calculable five-year statistics (1948-1952) show an over-all improvement (Table VI). The survival rate amongst all patients treated has risen from 62·2% to 66·7%.

In 1950 the International Gynæcological Congress recommended a new clinical classification for carcinoma of the

TABLE V.

Royal Prince Alfred Hospital, Sydney, N.S.W.: Five-Year and Ten-Year Survival Rates of Carcinoma Corporis Uteri, 1930 to 1952. (Compiled December, 1957.)

Treatment.	Five-Year Survivals.						Ten-Year Survivals.					
	Number.	Alive.	Post-Operative Deaths.	Other Deaths.	Lost.	Survival Rate.	Number.	Alive.	Post-Operative Deaths.	Other Deaths.	Lost.	Survival Rate.
Application of radium and surgery or surgery alone	205	148	4	43	10	72·2%	105	59	2	39	5	56·2%
Application of radium alone or radium *plus* deep X rays	35	4	3	27	1	11·4%	25	1	3	20	1	4·0%
Application of radium *plus* incomplete surgery or incomplete surgery alone ..	14	6	4	4	0	42·9%	7	1	3	3	0	14·3%
No treatment	7	0	0	7	0	—	5	0	0	5	0	—
Total	261	158	11	81	11	60·5%	142	61	8	67	6	43·0%

corpus uteri to compare the results of treatment by surgery and treatment by radiotherapy. This classification was adopted for use in the "Annual Report on the Results of Treatment in Carcinoma of the Uterus", edited in Stockholm, to which the Royal Prince Alfred Hospital contributes. The stage of each case is determined according to certain rules

TABLE VI.

Royal Prince Alfred Hospital, Sydney, N.S.W.—Carcinoma Corporis Uteri, 1948 to 1952: Survival Rate during Most Recent Five-Year Period.

Observation.	Five Years.
All patients examined with a view to treatment	119
All patients treated	117
Alive without recurrence	75
Alive with recurrence	3
Died of carcinoma	29
Died of intercurrent disease under five years	4
Lost or not followed up	8
Cure rate amongst all patients seen	63·0%
Survival rate amongst all patients seen	65·5%
Cure rate amongst all patients treated	64·1%
Survival rate amongst all patients treated	66·7%

at an examination prior to treatment; and this classification remains, no matter what is found at operation. Carcinoma of the corpus uteri is classified as follows:

Stage 0.

Stage I. The growth is confined to the uterus.
Group 1: operation advisable.
Group 2: bad operation risk.

Stage II. The growth has spread outside the uterus.

TABLE VII.

Royal Prince Alfred Hospital, Sydney, N.S.W.: Five Year Survivals in 261 Cases of Carcinoma of Corpus Uteri, 1930 to 1952.
(International Classification.)

Type of Carcinoma.	Number of Cases.	Alive with no Recurrence at Five Years.
Carcinoma Corpus Uteri		
Stage 0	4	3
Stage I:		
Group 1	200	139 (69·5%)
Group 2	16	1
Stage II	24	3
Total	240	143[1] (59·6%)
Carcinoma Corporis et Endocervicis	11	1
Carcinoma Uteri et Ovarii	6	3

[1] Eight other patients were alive with recurrence at end of five years.

If, at the first clinical examination, there is carcinomatous involvement of both the cervix uteri and the corpus uteri, or of both the ovary and the uterus, then the case is placed in a separate group—carcinoma corporis et endocervicis, or carcinoma uteri et ovarii.

Classification of the 257 cases in this series according to this system and the five-year survivals of each group are shown in Table VII.

When the statistics are considered, it should be realized that cancer in the body of the uterus occurs much later in life than cancer of the cervix, and that in the ten-year figures under other deaths consideration must be given to the scourges of old age.

Many of the pathological specimens, and all the paraffin-embedded sections and microscope slides of all cases and records of the growths, enumerated since 1930 are preserved and grouped in chronological order in the gynæcological department of the King George V Hospital and are available for study by any authorized student in this field of medicine, as well as by any general practitioner who wishes to improve his knowledge in the subject of womb cancer.

Carcinoma of the Vulva.

Characteristically, carcinoma of the vulva is a disease of the late post-menopause; 68% of cases occur between the ages of 60 and 80 years, the peak age incidence being 67 years.

There were 52 cases seen from 1950-1957, 50 being treated. These were staged according to the following criteria:

Stage I. Growth less than 2·5 centimetres in diameter, confined to vulva.

Stage II: Growth of 2·5 centimetres in diameter and/or spread to superficial set of lymph nodes on one or both sides.

Stage III. Growth with spread to intermediate or deep set of intrapelvic nodes and/or involvement of vaginal walls or anus or large nodal groin mass not fixed inoperably to vessels.

Stage IV. Growth with spread to involve bone locally or distant metastases or ulcerative nodal groin mass fixed to vessels.

TABLE VIII.

Stage.	Number of Cases.	Number of Deaths.	Absolute Survival Rate (Not Five Years).
Stage I	18	3	83%
Stage II	19	4	79%
Stage III	10	6	40%
Stage IV	3	3	—
All stages	52	16	69%

Node Involvement at Operation.

Node involvement found at operation was as follows:

Total operations	50	
Nodes involved	20	(40%)
Nodes not involved	30	
Superficial nodes only involved	14	(28%)
Superficial and deep nodes involved	5	(10%)
Deep nodes only involved	1	(2%)

Results of Treatment.

The results of treatment are shown in Table VIII.

Operative Procedures.

The following operative procedures were undertaken:

Extended radical vulvectomy with regional lymphadenectomy: *one stage, 38; two stages, 8; total 46.*

Perineo-ano-vulvectomy with lymphadenectomy and left iliac colostomy: three stages, 3.

Anterior pelvic exenteration: 1.

Outcome.

The total deaths from all causes numbered 16, made up as follows: (*a*) intercurrent deaths without recurrence, 5; (*b*) primary deaths, 1; (c) died of malignant disease, 10.

The number of patients surviving was 36.

The operability rate was 96%. The operative mortality rate was 2%. The absolute five-year survival rate was 60%.

Acknowledgements.

The staff pays tribute to the work of Dr. Malcolm Stening for preparing the statistics on carcinoma of the vulva, to Dr. F. Pigott for those on carcinoma of the cervix, and to Dr. Malcolm Coppleson for those on cancer of the body of the uterus. The staff wishes also to thank Miss M. Cunningham for her reliable secretarial work on behalf of the department.

Signed on behalf of the gynæcological staff of the King George V Memorial Hospital, Royal Prince Alfred Hospital

HERBERT H. SCHLINK.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE RESIDENT MEDICAL OFFICERS' ANNUAL ELECTION AT THE MELBOURNE HOSPITAL.[1]

[From the *Australasian Medical Gazette*, May 15, 1894.]

THERE is seldom a year that some hitch does not occur in the working of the Melbourne Hospital machinery, but the most awful contingency the Committee has had to face was that which occurred in connection with the most recent election held on April 10. It had to decide whether a lady graduate of the Melbourne University, who stood second on the honour list, and was, therefore, ex officio so to speak, entitled to become a resident medical officer at that noble institution for one year, was eligible or not, and only escaped from the difficulty by the Chairman's discovering a little flaw in Dr. Stone's claim to the post. The technicality consisted in the fact that Dr. Stone had not been a student of the Melbourne Hospital. The meanness and absurdity of utilizing it consists first in the agreement between the University on the one hand, and the Melbourne Hospital Committee on the other, being openly violated, for it has been a long-standing practice to appoint the first five honour "men" on the list of the last examination to the coveted posts, and Dr. Stone was second on the list. The possibility of a woman ever taking honours seems never to have occurred to the Dean of the Faculty of Medicine of the Melbourne University when this agreement was arrived at. The further meanness and absurdity in connection with this matter is that Dr. Stone could never have been a student at the Melbourne Hospital, because she was precluded from attending there when she first entered for medicine. Had not the staff of the Alfred Hospital gallantly come to the rescue at the time and taken charge of the lady students when they were debarred from the use of the Melbourne they would never have been able to graduate at all. The Alfred Hospital ladies have so far been very successful, Dr. Castilla having been recently appointed Resident Medical Officer to St. Vincent's Hospital, Melbourne: why then, should the Alfred not appoint its own residents from amongst the lady graduates trained within its walls, and so end a manifest injustice? Progress at the Melbourne Hospital it seems hopeless to look for.

[1] From the original in the Mitchell Library, Sydney.

Special Correspondence.

NEW ZEALAND LETTER.

The Cause of Facial Eczema in Sheep.

FACIAL ECZEMA is a disease which affects mainly sheep, though cattle may be affected, and the useful guinea-pig is susceptible to it under laboratory conditions; it is almost confined to the North Island of New Zealand. The external signs of the disease are jaundice and sores on the exposed parts of the body, especially round the face; these symptoms are attributed to liver damage and the circulation of photosensitizing breakdown products. The dangerous times are in the autumn when warm rains cause a flush of fresh young grass (rye grass areas in particular), and the only useful palliative has been to crowd sheep together to prevent them getting too much "toxic grass". Warnings are issued each season when conditions are thought to conduce to the appearance of facial eczema. Many people—farmers as well as scientists—have long suspected a fungus or other live product as the cause of this condition, but up to the present no success had attended this line of approach. However, an important advance is now announced by Dr. C. P. McMeekan of the Government Animal Research Station at Ruakura. The elusive toxic agent has been identified as the fungus *Stemphyllium botryosum*, though much detail has yet to be filled in—for example, the relative importance of spores, mycelium, or toxins produced by the fungus. The present success followed the observation of a farm hand, employed in cutting such "toxic" grass, that a fine black cloud followed his mower. Some mycelial growth was found at the roots of the grass, and a fine black deposit could be scraped off the blades of the mower. These items gave a positive empirical "beaker test" for toxicity, and cultures of the fungus after identification have yielded extracts which reproduce the disease in guinea-pigs and lambs.

Much remains to be done. The fungus is widespread—facial eczema fortunately is not. Various means by which this new discovery may be applied to control on the farm are being explored. The team of four special chemists and pathologists recently recruited in the United Kingdom to reach New Zealand early in 1959 will now have a much more promising task.

Correspondence.

THE PROSPECTS OF CANCER CURE.

SIR: Sir Macfarlane Burnet, in a recent Press interview on his return from abroad, is stated to have expressed the opinion that "a cure for cancer is never likely to be found". Such a statement, coming from such a source, cannot fail to have far-reaching repercussions on the public mind, and is of particular significance to practising members of the medical profession, who are perhaps better equipped than their purely academic colleagues to appreciate the importance of sustaining patients' morale.

I leave it to our National Health and Medical Research Council and other bodies engaged in cancer research to decide whether their efforts can be justifiably regarded with pessimism; but I feel that we have a special obligation to two classes of people—those who so splendidly supported the recent appeal for the Anti-Cancer Campaign, and who may well be wondering whether they should ask for their money back, and those who are suffering from cancer at the present time. I think we should seize every opportunity to remind these people that medical science has already found ways in which certain forms of cancer can be arrested, and in other cases, while an active cure cannot be achieved, a great deal can be done to combat and alleviate its effects; and that the medical profession will be undeterred by the prophets of gloom, and will never abate its efforts to add this dread disease to the list of those which have eventually been conquered by unremitting and optimistic medical research.

Yours, etc.,

H. CECIL COLVILLE,
President, Federal Council of the British Medical Association in Australia.

1045 Burke Road,
Hawthorn East,
Victoria.

September 23, 1958.

DIAGNOSTIC RADIOLOGY.

SIR: Konrad Röntgen's disease was suggested as a possible name for some cases of acute myeloblastic leukæmia by me (M. J. AUSTRALIA, August 9, 1958) and Dr. Mary Thornton's diverting comments (M. J. AUSTRALIA, September 20, 1958) are apposite and human. However, I violently disagree with her main conclusion, i.e., that "registration of radiographers is long overdue". Let us grant that (*a*) "ionising radiation has been shown conclusively to be leukæmogenic in man",[1] (*b*) "the incidence of leukæmia in radiologists is eight to ten times as great as in non-radiologists",[1] and (*c*) the three atomic bombs, used in anger, ended a destructive global war and produced 92 cases of leukæmia in Japan.[1] Then the total misery caused by radiation in the world in two decades is still less than the havoc attributable to accidental electrocution in any fortnight. And domestic gas being toxic and explosive, shall we also register Bunsen burner operators, i.e., most metropolitan cooks and students, Dr. Thornton? Furthermore, should we render unto Cæsar the power to set a series of long written examinations on the organic chemistry of combustion, the kinetics of heat and Van der Waal's mathematics (all of

[1] Wintrobe, M. M., "Clinical Hæmatology", Fourth Edition, page 912.

which can be unintelligently crammed and soon forgotten), before we register the humble housewife as competent to use that good servant but deadly master, fire?

> In passing by the side of Mount Thai, Confucius came on a woman who was weeping bitterly by a grave. The Master pressed forward and drove quickly to her; then he sent Tse-lu to question her. "Your wailing", said he, "is that of one who has suffered sorrow on sorrow." She replied: "That is so. Once my husband's father was killed here by a tiger. My husband was also killed and now my son has died in the same way." The Master said: "Why don't you leave the place?" The answer was: "There is no repressive government here." The Master then said: "Remember this, my children: repressive government is more terrible than tigers."

My contention is that the dangers of leukæmia are less terrible than the danger of even further increase of government control of the enthusiastic curiosity of youth. Already we have registration of nurses (over the dead body of Florence Nightingale), of physiotherapists, of dogs, of "medical persons", i.e., of you and of me, which distinction we share with dairy herds and second-hand dealers. Registration of radiographers would segregate another hungry conceited rabble of legally qualified monopolists, like the anonymous minions of the Repatriation Department and the Department of Mental Hospitals, and the lowly gang created by the pernicious system of intraprofessional espionage legalized by the *Workers' Compensation Act* with its approved (i.e., registered) medical referees. Meekness, not enthusiasm, is the first law of survival for a beginner dealing with any government department. Only someone with a perverted taste for martyrdom will fail to kow-tow to seniors who themselves bow very low indeed to the autocrat at the apex of the pyramid of bureaucracy. Under the slightest political duress the timid mind of any government servant would accept the example I gave as evidence of the production of leukæmia by X ray, unless legalistic proof to the contrary could be adduced. Yet no scientific conclusion could be made relating my late patient's leukæmia to his pilgrimage through the radiological supermarket of this world.

Do not you concede, Dr. Thornton, that, for example, Marie Curie, Paul Ehrlich and Best were unregistered "little titbits" when, playing with celestial fire, they made darkness light for many of the rest of mankind forever? Registration is a time-binding device. Let us leave youth and enthusiasm unfettered, for of such, and not of registered persons, is the Kingdom of Heaven.

Yours, etc.,

607 New South Head Road,
Rose Bay,
Sydney.
GODFREY HARRIS.

September 23, 1958.

SYSTEMIC LUPUS ERYTHEMATOSUS.

SIR: After reading the leading article on "Systemic Lupus Erythematosus" in the August 30 issue of THE MEDICAL JOURNAL OF AUSTRALIA, I would be grateful if you would publish the following comments. It would appear from this leading article that there is some unawareness of the part played by dermatologists in the history and therapy of this disease. I thoroughly agree that the condition is becoming "very much a matter for the general practitioner", which comprises another of many reasons why there should be a considerably greater time spent on the teaching of dermatology in our medical course. This receives added emphasis and importance when one reads in the leading article the following statement: "Faced with the syndrome, the physician must distinguish systemic lupus erythematosus from" four different conditions which are listed. There is, however, no mention of the two most important conditions from which it can be distinguished on occasion only with the greatest difficulty. This difficulty can be considerably greater than that caused by any of the conditions mentioned and may be encountered with dermatomyositis or generalized scleroderma.

At this stage may I, again with respect, draw attention to a statement in the interesting and instructive paper by Mackay in the same issue of THE MEDICAL JOURNAL OF AUSTRALIA. The statement reads: "If this concept is correct lupus erythematosus and other collagen diseases . . ." It is by no means generally accepted now that S.L.E. is a collagen disease. In fact, H. Montgomery, of the Mayo Clinic, one of the outstanding dermal histopathologists of today, has stated (and told me personally) that he can find no histopathological evidence at all to support such a concept. He is far from being alone in not accepting S.L.E. as a collagen disease.

I am further at variance with the statement that it has been regarded as "the concern only of the specialist in internal medicine until the last few years". In this regard, may I be permitted to draw attention to some pertinent facts in connexion with lupus erythematosus in general. At this stage I would recommend that those who are interested in the history and therapy of S.L.E. should read, among others, the excellent paper on this subject by Harvey *et alii*.[1] Here may be read such information as the following: A review of the historical development of our knowledge of S.L.E. serves to emphasize the remarkable variability in the clinical picture as evidenced by the number of years which passed before the protean manifestations could be grouped together as parts of a systemic disease. First to attract attention were dermal lesions of lupus erythematosus described under the term "erythema centrifuge" by Biett (a dermatologist) in 1928. Later, Hebra (another world-famous dermatologist) gave a more detailed description and noted two types: disk-like patches and detached or confluent lesions of smaller size. Kaposi (still another world-famous dermatologist) then designated the two forms described by Hebra as the discoid form and lupus erythematosus disseminatus. The first description of S.L.E. was made by Kaposi in 1872 (which date was mentioned in your leading article, but not the author or his specialty). He observed patients whose illness was characterized by fever, toxic manifestations and cutaneous lesions resembling those of erysipelas to which he gave the name "erysipelas perstans faceii". It was not until 1895 that a physician, "a specialist in internal medicine", came into the picture in the person of Osler, who emphasized the significance of the systemic manifestations of the disease, and the relationship of the visceral lesions to those in the dermis, and pointed out instances in which the disease ran its entire course to death without the development of cutaneous manifestations.

In 1904, Jadassohn (probably the greatest of all dermatologists to date) reviewed the disease, and referred to the frequency of involvement of the joints, serous and mucous membranes and kidneys, and also to constitutional manifestations such as fever and prostration. From then on until the present day a constant stream of papers on the subject has appeared from pens of dermatologists including Goeckerman, Arnold junior, Barnes, Moffatt, Lane, Weir, Bechet, Beerman, Belote, Bolgert, Brunsting, Casenave, Goldberg, Goldblatt, Gougerot, Haserick, Haxthausen, Johnson, Keil, Kierland, Madden, Montgomery, O'Leary, Pascher, Rein, Sawicky, Sequeira, Sezary, Sommerville, Stokes, Ingraham, Strakosch, Sundberg, Templeton, Tommasi, Urbach, Ward, Wells, Welsh and Wise, to mention only a few of them.

The discovery of the lupus erythematosus cell was made by Haserick, of Cleveland, Ohio, even though this discovery first appeared in the literature under the name of Hargraves and his associates. Again it was the dermatologists (in Great Britain) who first confirmed the chance discovery by Page of the beneficial effects of antimalarial drugs for chronic discoid lupus erythematosus, owing to the observation that patients who received "Atebrin" for rheumatoid arthritis became cleared of their skin lesions of lupus erythematosus. It was not at the time known that a Russian dermatologist had already discovered this fact about 10 years previously. Since then, newer antimalarials have been employed and pioneered almost entirely by dermatologists in their early stages, e.g., chloroquine, plaquenil, amiodiaquin etc. Even in classification, those formulated by dermatologists such as O'Leary, of the Mayo Clinic, are the ones in most common use today. Again, the use of steroid hormones in S.L.E. (which significantly prolong life and may even save it) was pioneered to a large extent by dermatologists who are still in the forefront with the exhibition of this therapy. To revert again to the early statement in the leading article that S.L.E. "has been regarded as the concern only of the specialist in internal medicine until the last few years", may I point out that it is only during the last few years that the specialists in internal medicine have become really interested in S.L.E. even to the extent of consulting and collaborating with their dermatological colleagues in its diagnosis and management. Prior to this, the condition fell mainly into the domain of the dermatologists for its identification and treatment, and still does in many leading clinics, notably in the U.S.A. Here in Sydney, collaboration between the internist physician and the dermatologist is now mainly in vogue, and would appear to offer the best over-all prospects for the patient.

Yours, etc.,

143 Macquarie Street,
Sydney,
J. C. BELISARIO.

September 12, 1958.

[1] *Medicine*, 1954, 33: 291.

Obituary.

CECIL CONRAD KLUG.

WE are indebted to Dr. T. L. Tyrer for the following appreciation of the late Dr. Cecil Conrad Klug.

Cecil Conrad Klug was born in Charlton, Victoria, on July 19, 1898, and died in Melbourne on January 19, 1958. His boyhood was spent in Queenscliff where his father, a well-known identity, was mayor for many years. He was educated at Melbourne Grammar School, and on leaving school enlisted and served in France as a private in the 59th Battalion. Returning to Australia, he commenced his medical course at the University of Melbourne, qualifying in 1928. Following residences at the (Royal) Melbourne, Women's and Prince Henry's Hospitals, he was appointed to the medical staff of the Repatriation Commission, taking up duties at Randwick Hospital in 1930, and he continued in the service of the Commission until the time of his death.

During this period he held appointments in repatriation hospitals in New South Wales, Victoria and Western Australia and, in later years, in medical administrative posts in the Victorian office and at headquarters. During World War II he utilized his annual recreation leave and any other time he could be spared from departmental duties to serve, with the rank of major, in field ambulances and camp dressing stations. He was a member of the Naval and Military Club, M.C.C., Kingswood and Queenscliff Golf Clubs and the Caulfield Returned Soldiers' Club.

For the last 14 years of his 28 years as an officer of the Repatriation Department, Cecil worked at the headquarters of the department in the capacity of a medical officer preparing final medical opinions for consideration by the Repatriation Commission. His opinions were respected by those with whom he himself consulted, as well as those who sought his advice, and his department has spoken in glowing terms of his application to duty and his efficiency at his work. He was a gentle man who was never known to utter a scathing or ill-natured criticism of those whose opinions differed from his. He enjoyed the simple, pleasant things of life and, in so doing, made those working with him feel that here was an honest man who gave the best he had and wished that he could give more.

He will be missed by his colleagues and by ex-servicemen generally. His long sympathetic service in the interests of ex-soldiers won for him the friendship of all with whom he came in contact. Cecil was extremely devoted to his family and their welfare. He is survived by his widow and son, Geoffrey (now in the fifth year of his medical course), to whom the deepest sympathy is extended.

ARTHUR BASIL CORKILL.

WE are indebted to Dr. Balcombe Quick for the following appreciation of the late Dr. Arthur Basil Corkill.

The recent death of Arthur Basil Corkill at the age of 59 marked the termination of a long and valued association with Alfred Hospital and the Baker Institute. Educated at the Melbourne High School and the University of Melbourne, he graduated M.B., B.S. in 1922 and was appointed a resident medical officer to the Alfred Hospital in May of that year. A fellow resident who was also later to gain high distinction was Rupert Willis, now Professor Emeritus of the University of Leeds. For part of Corkill's term of office as a resident he was associated with the late Dr. J. F. Mackeddie, who came to form a high opinion of his capabilities. About this time the establishment of a biochemistry department was under consideration, and a request was received from Dr. Mackeddie, then abroad, that Corkill should be seconded from further residential work at Alfred Hospital to study under Professor Maclean in his research laboratory at St. Thomas's Hospital. So highly, indeed, did Mackeddie rate Corkill that not only did he guarantee to meet all expenses of a year's study there, but also succeeded in interesting the late Mr. Thomas Baker to the extent of providing the establishment apparatus, and paying the first year's salaries of the new biochemistry department—the Baker Institute in embryo.

Upon his return to Australia in April, 1924, Dr. Corkill was appointed biochemist to the hospital, and in the following year he became associated with the asthma and other clinics in which his special knowledge might prove of value. But it was the establishment of the diabetic clinic in March, 1926, which opened up to him the field of work in which he was to so distinguish himself—that of carbohydrate metabolism. To this clinic, the first of its kind in Victoria, he was appointed physician-in-charge, thus combining the work of a clinician with research into the biochemical problems of the disease. Investigations were carried out at this time into the value of certain so-called "cures" for diabetes, prickly pear and *Vinca rosea*, but a more positive contribution was the compilation of brochures, for both physician and patient, giving in outline the methods practised in the diabetic clinic of Alfred Hospital and covering the use of insulin, then in its infancy.

Such was the arrangement until 1929, when he was granted leave to return to London to work under Sir Henry Dale in the National Institute for Medical Research. Thus began a happy period of collaboration lasting more than a year, of which his chief wrote of "the unqualified pleasure and advantage to have Dr. Corkill here". From this association there resulted various papers upon carbohydrate metabolism. A short period of further work in Germany preceded Corkill's return to Australia in 1930, as senior staff member in the Baker Institute under the first Director, Dr. Penfold. In this capacity he made a notable contribution to general physiology with a paper, in association with O. Tiegs, upon the effect of sympathetic nerve stimulation on the power of contraction of human muscle.

After the death of Dr. W. J. Penfold in 1938, Dr. Corkill was appointed Director of the Baker Institute. With the outbreak of war in the following year a period of added activity and responsibility began in an association with the Chemical Warfare Section of the Department of Munitions, lectures to practitioners upon chemical warfare and civil defence, and the production of certain essential drugs in short supply. So continued a busy and useful life until retirement from the directorship of the Institute in 1949 was necessitated by illness. No longer was it possible for him to take any more active part in its affairs than that of a consultant, nor was it possible for him to play golf or to fish, his former hobbies.

Mention has already been made of two notable contributions to physiological and biochemical literature, and Corkill's name will always be associated with pioneer work in relating the pituitary gland with control of carbohydrate metabolism and the metabolism of fructose. Several of Corkill's contributions to medical scientific literature are of a fundamental nature and have been incorporated in well-known text-books of physiology. His scientific attainments gained him both a doctorate in science and a fellowship of The Royal Australasian College of Physicians. To those who were privileged to know Dr. Basil Corkill he will always be remembered for his essentially kindly nature, and his assistants and colleagues have had every reason to be grateful to him for help and encouragement in their work. Many of his old patients of the diabetic clinic of 1926-1928 continued to consult him in the ensuing years. He was a generous helper to anyone in need. His loss is greatly felt by his friends, and they wish to extend their sympathy to his widow and daughter in their bereavement.

NAPHTALI GOLDMAN.

WE are indebted to Dr. M. E. Cameron for the following appreciation of the late Dr. Naphtali Goldman.

The loss of Dr. N. G. Goldman and his wife on November 30 last in a motor-car accident, while returning from a psychiatry conference in Hobart, was a great blow to their many friends. It marked the end of a brief life intensely lived and filled with a variety of interests. The end of a day's consultations frequently heralded the beginning of voluntary work elsewhere, and many nights were devoted to work at the Spastic Centre, and to meetings of the Jewish National Fund Commission and the Australasian Association of Psychiatrists, for both of which he was secretary.

His early interest in psychiatry showed itself when, eighteen months after graduation in 1946 from the Queensland University, he became psychiatric registrar at the Brisbane General Hospital. In 1950 he entered private practice at the Brisbane Clinic, and two years later, with his wife Gulida, went to London, where he had a year's post-graduate training at the Maudsley Hospital. He passed the first part of the Diploma of Psychological Medicine, and a week later sat for and passed the second part. This climaxed a year of study, and in the subsequent months, before returning to Australia, he was able to relax and indulge in the rich cultural life which London offers. Across Waterloo Bridge to the Festival Hall and the Old Vic, up Shaftsbury Avenue with its many theatres, or down through St. James' Park to the St. James—these were his favourite haunts, preceded by dinner at the Ivy or the Boulestin, if finance allowed it.

Norm returned home to Brisbane in 1954 and entered private practice, one of his first purchases being an electro-encephalographic machine. Appointments at the Brisbane General and Children's Hospitals, Repatriation Hospital and Spastic Centre, as well as lecturing at the University, kept him busy, but he could still find time to relax. Fortunate were those who were invited to sit at his table and partake of the excellent cuisine prepared with such care by his wife. With candles gleaming in the polish of the antique Windsor table, the stage was set for a delightful evening. After coffee, Norm would bring out some of his favourite Bach and Beethoven records, and so the evening would slip away.

He leaves a daughter, Jael, only two years old, who is being brought up with his sister's children. Both he and his wife leave behind a host of pleasant memories, and their loss has been most deeply felt.

JOHN JOSEPH LUDDY.

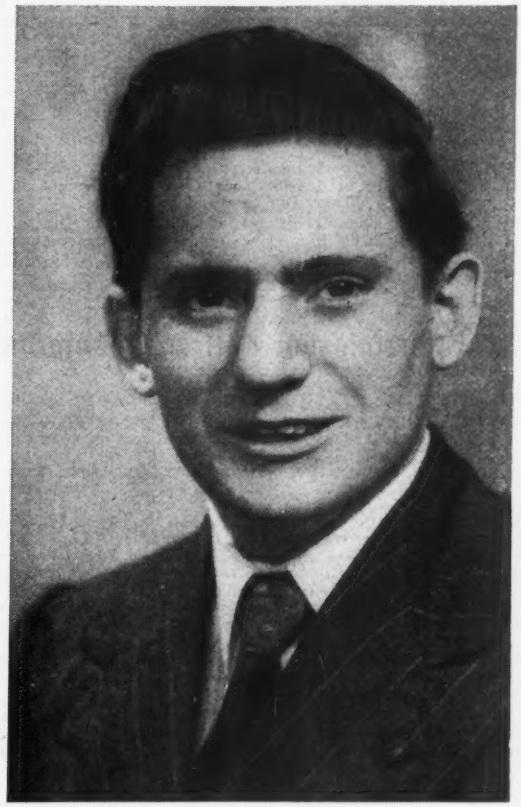
WE are indebted to Dr. Felix Arden for the following notice of the career of the late Dr. John Joseph Luddy.

John Joseph Luddy, who died recently in Brisbane at the age of seventy-one, was in his younger days a prominent Brisbane surgeon. Born at Gympie, where his father was a director of mining companies, Dr. Luddy was educated at Nudgee College and gained a bursary which took him to St. John's College, University of Sydney. After graduating at the age of twenty-four, he served as an R.M.O. in Queensland and later became superintendent of the Mount Morgan Hospital, where in due course he married the matron, Miss Margaret Aland. Post-graduate work followed in Edinburgh and later in Cambridge, where he took a degree in radiology, after which he studied at Lausanne, gaining his doctorate of medicine. On his return to Brisbane, Luddy commenced practice in the city and continued to work at the same address for the remainder of his life. Although he held no public hospital appointments, he had a substantial practice and was also for many years an anatomy demonstrator at the medical school. An athlete in his youth, he played football for New South Wales against England while a student at the University of Sydney. He is survived by his wife, to whom our sympathy is extended.

KENNETH JAMES ELLIS.

WE are indebted to Dr. J. J. Smyth for the following appreciation of the late Dr. Kenneth James Ellis.

Ken Ellis was fatally injured on the dangerous Newcastle to Sydney road on Sunday, June 30, 1958, and died less than three days later in Royal Newcastle Hospital. This gifted young man had the best of a brilliant career before him. A Novacastrian, he returned to Newcastle for his resident training. His excellence as an R.M.O. resulted in his appointment as Urology Registrar in 1957, an appointment which produced a happy result for everybody—his hospital, his colleagues, his teachers, his assistants, nursing and lay, and his patients. His technical ability, though masterly, was quite overshadowed by his intellectual grasp of surgery as a whole. That the great pride of his father, for many years honorary urologist, should be turned to equally intense grief, added not a little to the sorrow of all concerned. It speaks volumes for the care and understanding he must have lavished on his patients that so many have already expressed grief at his passing. The Newcastle police saw fit to halt the city that his funeral might pass by—a great tribute to



a man of 29 years. Large numbers of nursing and ambulance staff attended, to show that it was possible both to work for and to love this man. All those free to do so lined the street as the cortege passed the hospital he served so well.

His hospital and his specialty are immeasurably the poorer for his passing. Despite his youth, he showed unmistakable signs of probing beyond the limits of present knowledge. His transparent honesty and incisive thinking would not allow him to suffer tradition which had outworn its usefulness. To his wife, also gravely injured, and to his parents and family goes our deepest sympathy.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE following additions and amendments have been made to the Register of Medical Practitioners for New South Wales in accordance with the provisions of the *Medical Practitioners Act*, 1938-1958.

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1*a*) of the Act: Fleming, Hugh Alexander, M.B., Ch.B., 1947 (Univ. New Zealand), M.D., 1952 (Univ. New

Zealand), M.R.C.P. (London), 1955; Lie, Kwie Lian, M.B., B.S., 1955 (Univ. Melbourne), B.Sc., 1953 (Univ. Melbourne); Nicholls, Jean Goodair, M.B., B.S., 1926 (Univ. Melbourne); Nicholls, Ralph Whitburn, M.B., B.S., 1925 (Univ. Melbourne); Robinson, John Jefferson, M.B., B.S., 1956 (Univ. Melbourne); Rodan, Brian Alexander, M.B., B.S., 1955 (Univ. Melbourne); Stretton, Philip John Crawford, M.B., B.S., 1943 (Univ. Melbourne).

Registered medical practitioners who have complied with the requirements of Section 17 (3) and are registered under Section 17 (1*b*) of the Act: Duke, Harold Price, M.R.C.S. (England), L.R.C.P. (London), 1952; Fischer, Emanuel, L.A.H. (Dublin), 1950, L., L.M., R.C.P. (Ireland), 1951, L., L.M., R.C.S. (Ireland), 1951, D.P.M., R.C.P. & S. (Ireland), 1956. Henderson, Sidney Peter Addison, M.B., Ch.B., 1948 (Univ. Edinburgh); Hunter, William Home, M.B., Ch.B., 1943 (Univ. Edinburgh); Mitchell, John, L., L.M., R.C.P. (Ireland), 1925, L., L.M., R.C.S. (Ireland), 1925.

Registered medical practitioner who has complied with the requirements of Section 17 (3) and is registered under Section 17 (2A) of the Act: Sandler, Joseph, M.D., 1926 (Univ. Leipzig).

The following has been issued with a licence in accordance with the provisions of Section 21C of the Act: Strait, Laura Meller, M.D., 1923 (Univ. Budapest).

The following has been issued with a Certificate of Regional Registration in accordance with the provisions of Section 21A of the Act: Dax, Albert Andrew, 1934 (Univ. Budapest).

Royal Australasian College of Surgeons.

PRIMARY EXAMINATION FOR FELLOWSHIP OF THE ROYAL AUSTRALASIAN COLLEGE OF SURGEONS.

A PRIMARY EXAMINATION in anatomy (including normal histology) and applied physiology and the principles of pathology will be conducted in Melbourne in March, 1959, for the fellowship of the Royal Australasian College of Surgeons. The written paper will be held on Thursday and Friday, March 5 and 6, 1959. The examination is reciprocal with the primary examinations for fellowship of the Royal College of Surgeons, England, the Royal College of Surgeons, Edinburgh, the Royal College of Surgeons in Ireland, the Royal Faculty of Physicians and Surgeons of Glasgow, and the College of Physicians and Surgeons of South Africa. Each examination is open to graduates of not less than one year's standing of a medical school approved by the Council of the College for the purpose.

Candidates must submit evidence of their qualification and the date of acquirement thereof. Forms of application for admission to the examination may be obtained from the Examination Secretary, Royal Australasian College of Surgeons, Spring Street, Melbourne, Victoria. The fee for admission or readmission to the examination is £26 5s., Australian currency (*plus* exchange on cheques drawn on banks outside Melbourne). Candidates from New Zealand desirous of entering should forward their remittance in favour of the Royal Australasian College of Surgeons by bank draft drawn on Melbourne. The fee must be forwarded with the form of application so as to reach the Examination Secretary at his office in Melbourne not later than January 23, 1959. It is stressed that entries close at the College office in Melbourne on January 23, 1959, and late entries cannot be accepted.

FACULTY OF ANÆSTHETISTS.

Primary Examination for Fellowship of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons.

A PRIMARY EXAMINATION on anatomy, physiology, pharmacology and pathology will be conducted in Melbourne in March, 1959, for the fellowship of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons. The written papers will be held on Thursday and Friday, March 5 and 6, 1959. The examination is open to graduates of not less than one year's standing of an approved medical school. Candidates must submit evidence of their qualifications and date of acquirement thereof. Forms of application for admission to the examination may be obtained from the Examination Secretary, Faculty of Anæsthetists, Royal Australasian College of Surgeons, Spring Street, Melbourne, Victoria. The fee for admission or readmission to the examination is £26 5s., Australian currency (*plus* exchange on cheques drawn on banks outside Melbourne). Candidates from New Zealand desirous of entering should forward their remittance by bank draft drawn on Melbourne in favour of the Royal Australasian College of Surgeons Trust Account. The fee must be forwarded with the form of application so as to reach the Examination Secretary at his office not later than January 23, 1959. It is stressed that entries close at the Faculty office in Melbourne on January 23, 1959, and late entries cannot be accepted.

Post-Graduate Work.

ROYAL PRINCE ALFRED HOSPITAL: EAR, NOSE AND THROAT DEPARTMENT.

Seminar Programme, 1958-1959.

THE staff of the Ear, Nose and Throat Department will conduct a seminar on the second Saturday of every month at 8 a.m. in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital. The main speaker will not exceed forty minutes, and there will be a discussion at the conclusion of his remarks. All medical practitioners and clinical students are invited to attend.

The subjects at the first three meetings will be as follows: October 11, "Simple Tumours of the Larynx", Dr. B. P. Scrivener; November 8, "Nasal Polypi and the Place of External Ethmoidectomy", Dr. Volney Bulteau; December 13, "Tumour of the Ear", Dr. J. H. Lancken.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes etc. are published in the *Commonwealth of Australia Gazette*, No. 44, of August 14, 1958.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).

To be Temporary Major, 2nd June, 1958.—2/40187 Captain F. A. Lilier.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 1/33098 Captain E. F. Reye is confirmed.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/19012 Major C. Clifton-Smith is appointed to command 8th Field Ambulance, and to be Temporary Lieutenant-Colonel, 15th May, 1958.

2/70937 Lieutenant-Colonel A. L. Hellestrand relinquishes command of 8th Field Ambulance, 14th May, 1958, and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Eastern Command), 15th May, 1958.

2/50434 Captain R. J. M. Dunlop is appointed from the Reserve of Officers, 30th April, 1958.

2/127030 Honorary Captain C. A. Shearer is appointed from the Reserve of Officers, and to be Captain (provisionally), 30th May, 1958.

The provisional appointment of 2/146609 Captain (provisionally) A. E. Cronin is terminated, 14th April, 1958. To be Lieutenant-Colonels, 14th July, 1958: Majors (Temporary Lieutenant-Colonels) 2/100752 R. D. Rothfield and 2/147950 C. E. M. Gunther. To be Captain (provisionally), 15th April, 1958: 2/146609 Anthony Earl Cronin.

Southern Command.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 3/101836 Captain G. R. McLeish is confirmed. 3/101932 Captain M. N. Lolagis is appointed from the Reserve of Officers, 14th June, 1958.

Western Command.

Royal Australian Army Medical Corps (Medical).—5/32082 Captain W. B. C. Gray is appointed from the Reserve of Officers, and to be Temporary Lieutenant-Colonel, 11th June, 1958.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

Southern Command.—To be Honorary Captain, 2nd June, 1958: David Ephraim Yoffa.

The following officers are placed upon the Retired List with permission to retain their rank and wear the prescribed uniform, 31st August, 1958:

Northern Command. — Lieutenant-Colonel (Honorary Colonel) T. A. Parry.

Southern Command.—Captain A. E. Brauer.

Southern Command.—The following officers are retired, 31st August, 1958: Honorary Captains L. J. Gurry, H. O. Johnston, H. H. Martin, C. H. Prouse, L. Rabinov and R. R. Webb.

Notes and News.

Pfizer Research Fellowship (Overseas).

It is announced that Dr. S. Gershon, of Melbourne, has been awarded the Pfizer Fellowship for Research (Overseas) in Clinical Medicine for 1959.

The London Medical Exhibition.

The 1958 London Medical Exhibition will take place from November 10 to 14 at the Royal Horticultural Hall, Westminster. The Exhibition is the forty-second since that first held in 1905 and will be opened by Sir Roy Cameron, K.B., F.R.C.P., F.R.S., Professor of Morbid Anatomy, University College Hospital, London. A comprehensive range of drugs and medical specialities, surgical, medical and hospital apparatus and instruments, technical literature, research apparatus, etc., will be on view. A selection of technical medical films will be shown each day during the exhibition; a programme of these will accompany the invitation tickets. An item of special interest this year will be a collection of medical prints, by great artists of the past, which will be on view. Admission is extended to doctors, surgeons, pharmacists and other senior hospital officers and technicians, as well as purchasing agents and other senior personnel connected with medical practice. Visitors from overseas are welcome. Invitations may be obtained by writing to 200 Bishopsgate, London, E.C.2.

Services Canteens Trust Fund Post-Graduate Scholarships.

The trustees of the Services Canteens Trust Fund are inviting applications for two post-graduate scholarships, one for study overseas and the other for study at an Australian university. The fields of study in which the scholarships may be awarded are as follows: (*a*) For study overseas: (i) any course at any approved university throughout the world; (ii) aeronautics in England or America; (iii) travelling scholarship in any field; an applicant wishing to pursue any other branch of study may apply to the trustees for a scholarship in that field. (*b*) For study in Australia: study or research in any approved subject at any Australian university.

The scholarship for study overseas is valued at £A1000 *per annum*. The scholarship for study in Australia is valued at £800 *per annum*. Both scholarships will be tenable for a period of up to three years.

The scholarship is open to a child (including stepchild, adopted child or ex-nuptial child) of a person who was at any time between September 3, 1939, and June 30, 1947, (*a*) a member of the Naval, Military or Air Forces of the Commonwealth; or (*b*) a member of any nursing service or women's service attached or auxiliary to any branch of the Defence Force of the Commonwealth; or (*c*) members of the canteens staff of any ship of the Royal Australian Navy, and any person duly accredited to any part of the Defence Force who served in an official capacity on full-time paid duty.

Selection will be entirely on merit and will be competitive. A scholarship will be granted only to an applicant who, in the opinion of the trustees, has outstanding ability, is of suitable character, and is likely to obtain lasting benefit for himself or herself and for Australia by further study.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 20, 1958.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	3	8(3)	3(2)	..	..	..	..	..	14
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	7	..	7
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	1	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4	10(7)	8(6)	..	..	..	9	2	33
Diphtheria	4	..	..	..	1(1)	..	..	..	5
Dysentery (Bacillary)	..	3(1)	1(1)	3(3)	4(4)	..	..	..	11
Encephalitis	..	2	..	..	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1	..	..	..	..	..	..	1
Infective Hepatitis	106(40)	22(11)	9(4)	3(2)	1(1)	1	..	1	143
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	1	..	..	..	..	..	..	..	1
Malaria	..	..	1(1)[2]	..	1(1)[2]	..	..	..	2[2]
Meningococcal Infection	1(1)	1(1)	..	..	..	..	..	..	2
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	3(3)	..	..	..	..	..	..	4
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	50(44)	..	8(6)	140(122)	1(1)	..	14	213
Salmonella Infection	..	..	..	2(2)	..	..	..	..	2
Scarlet Fever	14(8)	9(8)	4	5(4)	8(8)	1	..	..	41
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1(1)	1	..	1(1)	..	..	..	3
Trachoma	..	..	..	..	11	..	..	..	11
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	25(18)	8(5)	8(3)	12(5)	15(9)	3	..	..	71
Typhoid Fever	..	..	1(1)	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.
[2] Source of infection outside Australia.

The scholarships will not necessarily be awarded each year. The following points will be taken into consideration in determining the award of the scholarships: (i) academic career; (ii) ability for research work; (iii) character; (iv) the future value to Australia of the subject of research selected. The selection each year of the scholars to be awarded the scholarships will be made from all applications received from eligible persons by the prescribed closing dates.

Applications must be lodged with the General Secretary, Services Canteens Trust Fund, Victoria Barracks, St. Kilda Road, Melbourne, by the prescribed closing date. Applications should be transmitted through the Regional Secretary in your State. Applications for the scholarship for study overseas close on November 1, 1958. Applications for study in Australia close on January 10, 1959.

Application forms and any further information may be obtained from the General Secretary or from the Regional Secretary of the Services Canteens Trust Fund in your State. The addresses of Regional Secretaries are as follows: Victoria Barracks, Brisbane; 84 Pitt Street, Sydney; Victoria Barracks, Melbourne; 22 Grenfell Street, Adelaide; Swan Barracks, Perth; Anglesea Barracks, Hobart.

Fairfax Reading Memorial Prize.

The Council of the Dental Alumni Society of the University of Sydney announce that the Fairfax Reading Memorial Prize for 1958 has been awarded to Dr. H. R. Sullivan, Assistant Director, Institute of Dental Research, Sydney, for his outstanding contributions to the knowledge and understanding of dental science, and service over many years to the dental profession. The Fairfax Reading Memorial Prize is awarded biennially.

Notice.

THE CHILDREN'S MEDICAL RESEARCH FOUNDATION.

THE following is a list of donations to the Children's Medical Research Foundation of N.S.W. received from members of the medical profession during the period from September 17 to 23, 1958.

Dr. R. Hertzberg: £50.
Dr. A. Distin Morgan: £25.
Drs. S. W., N. G. and D. A. Dobell-Brown: £21 7s. 6d.
Drs. J. F. Ackary, N. M. Nelson and B. Leigh: £15 15s.
Dr. and Mrs. H. O. Raggatt, Dr. and Mrs. J. R. Nelson, Dr. J. W. Knox, Dr. G. M. Purchas, Dr. J. C. Quoyle, Dr. R. A. G. Holmes, Dr. R. S. Day: £10 10s.
Dr. A. L. Bryant: £10.
Dr. P. E. Walton-Smith: £6.
Dr. Eleanor Arnst: £5 5s. 6d.
Dr. G. I. Wade, Dr. B. N. Beirman, Dr. I. H. R. Wonders, Dr. R. B. Pilcher, Dr. J. M. Nield, Dr. J. D. Benson, Dr. J. B. Wilson, Dr. G. M. B. Hales, Dr. D. Patrick: £5 5s.
Dr. G. P. Dodd, Dr. T. J. Lowe, Dr. V. J. McGovern: £5.
Dr. and Mrs. O. Rychter, Dr. M. Joseph: £3 3s.
Dr. Doris V. Coutts: £3.
Dr. John Glenton Watson, Dr. N. Watts, Dr. T. Pain, Dr. K. Blum, Dr. R. H. Brent: £2 2s.
Dr. Alan T. Clements, Dr. K. A. Blakey, Dr. K. G. Outhred: £2.

Previously acknowledged: £5936 4s. 3d. Total received to date: £6231 2s. 9d.

Deaths.

THE following deaths have been announced:

FIGTREE.—Edward Richardson Figtree, on September 28, 1958, of Hurstville, New South Wales, at sea.

STOKES.—Frank Oliver Stokes, on September 27, 1958, at Wentworth Falls, New South Wales.

CHERRY.—Alan Percival Cherry, on September 11, 1958, at Largs Bay, South Australia.

WEST.—Gordon Roy West, on September 17, 1958, at Erindale, South Australia.

MATHEWS.—Samuel Mathews, on September 17, 1958, at Kalgoorlie, Western Australia.

OFFICER.—Robert Officer, on September 22, 1958, at Canterbury, Victoria.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Brien, William Robert, M.B., B.S., 1956 (Univ. Sydney), Royal Newcastle Hospital, Newcastle.

Hensley, William Joseph, M.B., B.S., 1950 (Univ. Sydney), M.D., 1958 (Univ. Sydney), M.R.A.C.P., 1955, University of Sydney, Sydney.

Diary for the Month.

OCT. 13.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
OCT. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee; Organization and Science Committee.
OCT. 15.—Victorian Branch, B.M.A.: Clinical Meeting, Prince Henry's Hospital.
OCT. 15.—Western Australian Branch, B.M.A.: General Meeting.
OCT. 16.—Victorian Branch, B.M.A.: Executive Meeting.
OCT. 17.—New South Wales Branch, B.M.A.: Ethics Committee.
OCT. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales. The Maitland Hospital.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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